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A CONTRIBUTION TO THE ANATOMY AND SURGERY OF THE TEMPORAL BONE.

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The recent additions to the symptomatology and diagnosis of complications and sequelæ of middle-ear disease, with the resulting surgical interference in deep-seated affections, have made it necessary to acquire a more intimate knowledge of the landmarks of the ear and its surrounding structures. The present article, with the accompanying charts drawn from dissections on the cadaver, is intended to fill a requirement still existing in our medical literature and to serve as a guide for improved technique in the future for attacking the temporal bone and vital parts in its immediate neighborhood.

In the comparatively simple procedure of entering the mastoid antrum an incision through the skin, fascia, and periosteum, beginning behind the attachment of the auricle, at a point corresponding to the upper wall of the external auditory meatus and passing over the middle of the mastoid process to its tip, will suffice if the tissues are drawn forward to expose sufficient bone to appreciate the landmarks necessary for this operation. In the more extensive procedure of attacking the middle ear and its adjacent parts, a longer incision is necessary. The incision begins at a point above the ear sufficiently far back to avoid the temporal artery, then courses downward ½ to 1 cm. behind the attachment of the auricle, in order to avoid severing the

posterior auricular artery, and ends at the tip of the mastoid process (Fig. 1).

When the tissues are dissected and retracted a field will be exposed in which the entire outer and middle ear, as well as the mastoid antrum and the sigmoid flexure of the lateral sinus, can be reached (Fig. 2). Above the temporal ridge this incision should pass through skin alone, exposing the temporal fascia covering the temporal muscle; this should not be severed. Below the ridge it should pass directly to the bone of the mastoid process. The anterior flap should contain the auricle with the periosteum from the mastoid process and the entire soft parts of the external auditory meatus, the periosteum of the meatus remaining continuous with that covering the mastoid process. On elevating the periosteum and retracting the tissues still covering the process behind, an area will be exposed sufficient for the most radical operation on the temporal bone, even to the extent of its entire removal.

The following are the landmarks visible from above downward (Fig. 2): Above the temporal ridge or crest is the fascia covering the temporal muscle. The crest is the continuation backward of the zygomatic arch and affords attachment to the fascia as well as the temporal muscle, and corresponds in height to the upper wall of the bony auditory canal; it forms the division line between the squamous and mastoid portions of the temporal bone, and serves as a landmark for opening the mastoid antrum and lateral sinus.

In a simple mastoid operation the external opening should remain below this crest in order to avoid entering the cerebral cavity.

Below the crest and in front of the mastoid process is seen the external auditory meatus, a long, funnel-shaped canal, the walls of which are formed by the tympanic plate. The free margin of this plate (the auditory process) affords attachment to the cartilage of the ear.

In the depth of the meatus is seen the tympanic membrane or ear drum, lodged in a ring of bone with the manubrium or handle of the malleus, attached to and shining through its upper half, slanting from above and in front downward and backward. The upper portion of the membrane is thrown into folds by the outward projection of the processus brevis of the malleus, which springs from the upper part of the manubrium close to the tympanic ring. The portion of the membrane thus affected is called Shrapnell's membrane.

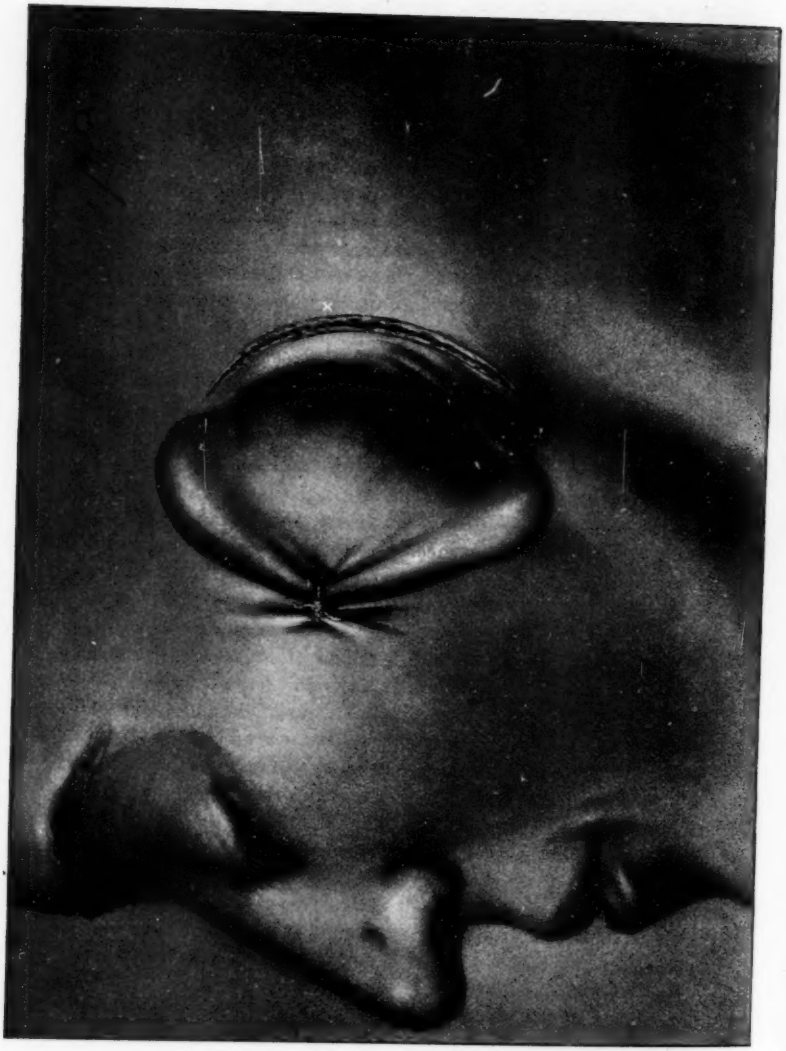
On removing the tympanic membrane from its ring of bone and from its attachment to the malleus, the tympanic cavity or middle ear is exposed and the following points of interest noted (Fig. 3): In the upper half of the cavity are seen anteriorly the manubrium, projecting downward and slightly backward, with the processus brevis at its upper end close to the rim of the bony canal. The processus longus of the incus is situated half a millimetre behind and parallel to the manu-

brium, and has its lower end attached to the stapes. The lower half of the cavity presents a rounded, glistening eminence, called the promontorium, and an opening directly behind it called the fenestrum rotundum. The latter opens into the cochlea, of which the promontorium represents the first turn.

In order to expose the tympanic cavity or middle meatus more thoroughly, a part of the superior and posterior walls of the external meatus can be removed (Fig. 4). The tympanic cavity (as seen in the last figure) has its upper part, the atticus, hidden behind the inner portion of the upper wall of the external auditory meatus. Hence, the upper wall of the meatus corresponds to the outer wall of the atticus, and with the procedure just mentioned the atticus is exposed.

The atticus contains the heads and bodies of the malleus and incus, and the removal of its outer wall shows these bones *in toto*. Besides these structures the tensor tympani muscle can be seen anteriorly emerging from its canal and becoming inserted into the neck of the malleus. The short process of the incus is seen projecting back into the aditus, while the long process descends to become attached to the stapes. Beneath the short process of the incus the chorda tympani nerve emerges from the facial canal in the posterior wall. It crosses the long process of the incus and disappears behind the malleus. When this nerve is injured accidentally or otherwise, the sense of taste for the corresponding side of the tongue is lost. Directly internal to the tip of the long process of the incus lies the stapes placed at right angles to it. To the neck of the latter is attached the stapedius muscle, which consists of minute fibres 1 to 2 mm. in length coming from the pyramidal-shaped cavity in the posterior wall of the middle meatus. In the background, portions of the inner wall of the middle ear are visible. Directly above the stapes and behind the incus is the projection of bone covering the facial nerve. Below the stapes, the promontorium and fenestrum rotundum are again seen as before.

At the upper posterior angle of the entrance to the bony meatus is a spicule of bone known as the suprameatic spine (Figs. 2 to 5). This is of importance in the simple mastoid operation, as it is prominent in most skulls, and when felt, serves as a landmark, being the most anterior point to which the tissues should be dissected, and also the point 1 cm. behind which the opening for entering the atrium should be begun. The mastoid process, of which the temporal ridge forms the base line, has been denuded of periosteum. Near its posterior border is situated the mastoid foramen, through which one of the emissary veins of the lateral sinus passes. Below, the process has the sternocleidomastoid muscle attached to it. The fibres of this should be left intact when these parts are exposed, excepting in those instances in which their presence interferes with the thorough exploration of the mastoid cells.



The nature of the bony structure of the process varies greatly in different subjects, being very compact tissue (small celled or diploic) in some and cellular (large celled or pneumatic) in others.

To reach the antrum, the chisel or burr drill must be placed at a point 1 cm. behind the suprameatic spine, and keeping below the temporal crest, or the upper wall of the meatus, must penetrate a mass of bony tissue to a depth varying from 1 cm. to 2 cm. in a direction inward, forward, and slightly upward, corresponding to the direction of the external auditory canal. The position of the antrum varies somewhat. Although it is generally situated about ½ to 1 cm. behind the outer opening of the auditory canal, it is sometimes found almost directly internal to its upper wall. The depth at which the antrum is met also varies, but it is safe to say that if the instrument penetrates deeper than 1½ cm., and be directed too far forward or downward, the horizontal semicircular canal or the aqueductus Fallopii will be encountered (Fig. 7). If the former were opened in a purulent otitis media the pus would travel along it to the vestibule and from there into the internal auditory meatus, producing a pachymeningitis or extradural (epidural) abscess of the posterior fossa of the skull; or from the vestibule through the perpendicular semicircular canal, which if accompanied by erosion of its bony covering would lead to involvement of the meninges of the middle fossa. The same would hold good for the posterior semicircular canal affecting the posterior fossa.

If the latter (the aqueductus Fallopii) were opened an inflammation of the facial nerve which is contained therein would result, producing paralysis of that side of the face. The inflammatory process might also find its way through the entire canal to the internal auditory meatus, causing a pachymeningitis or extradural abscess as mentioned above; or, travelling along the nerve to its cerebral attachment, would produce a meningitis or subdural (intradural) abscess. The direction of the penetrating instrument must also be forward, in order to avoid injuring the lateral sinus.

For extensive dissections on the mastoid process, where involvement of the antrum as well as the lateral sinus and the mastoid cells is suspected, a division of the process into four equal parts suggested itself to Dr. Hartley, and the following procedure has been evolved[1] (Figs. 3, 4, and 5): The temporal ridge, or a line continuous with the zygomatic arch, is taken as the upper boundary; the anterior border of

[1] In Chipault's "Surgery" reference is made of the division of the mastoid process for the purpose of locating the lateral sinus.

EXPLANATION OF FIG. 1.

Line of incision for radical operations. × Point from which incision for "mastoid operation" is made.

the mastoid process, as the anterior boundary; a line drawn vertically from the junction of the posterior border of the mastoid process where it meets the occiput, as the posterior boundary; and an imaginary line drawn backward from the tip of the mastoid process, as the lower boundary of a quadrangle. On dividing this into four equal parts it was found that in almost every instance the upper anterior quadrant opened into the mastoid antrùm, the upper posterior quadrant opened into the lateral sinus, and the two lower quadrants into mastoid cells. The lower posterior quadrant also opens into the descending limb of the lateral sinus if gone into sufficiently deep.

In permitting a wall of bone to remain separating the anterior and posterior quadrants, a safeguard is established which prevents the infectious discharge which might be found in the anterior quadrant (antrum), entering and setting up a similar process in the posterior quadrant with its lateral sinus, providing this has been exposed and found to be healthy and patent.

In this way, if any doubt exists as to the extent of infection, the entire surface of the mastoid can be immediately mapped out, and the upper anterior quadrant opened first to determine if the antrum is involved (Fig. 4). If this be so and the mastoid cells themselves contain pus, one or both lower quadrants can be opened and evacuated. If the process is very extensive, and there is reason to suspect an infected thrombus in the descending limb of the sigmoid flexure of the lateral sinus, which is the most frequent site for a beginning thrombus, the upper posterior quadrant can be gone into, the sinus punctured with a hypodermic needle or incised, if sufficiently exposed, and the nature of its contents determined. The bridges of bone between the quadrants have the advantage over a continuous bony wound, made by chiselling off the entire outer surface of the mastoid, as performed by many surgeons, on account of the support given the tissues which preserve the original contour of the parts, and the barriers which they form between infected and non-infected areas.

The descending limb of the lateral sinus is met at a depth ranging from ½ to 1 cm., and is usually seen taking a somewhat slanting course from above and behind, down and forward; it then dips in forming the sigmoid flexure. The sinus generally fills the upper posterior quadrant, but at times it will be seen only in the posterior half or two-thirds of the quadrant, and in these cases the quadrant can be enlarged posteriorly. Frequently the mastoid vein can be seen

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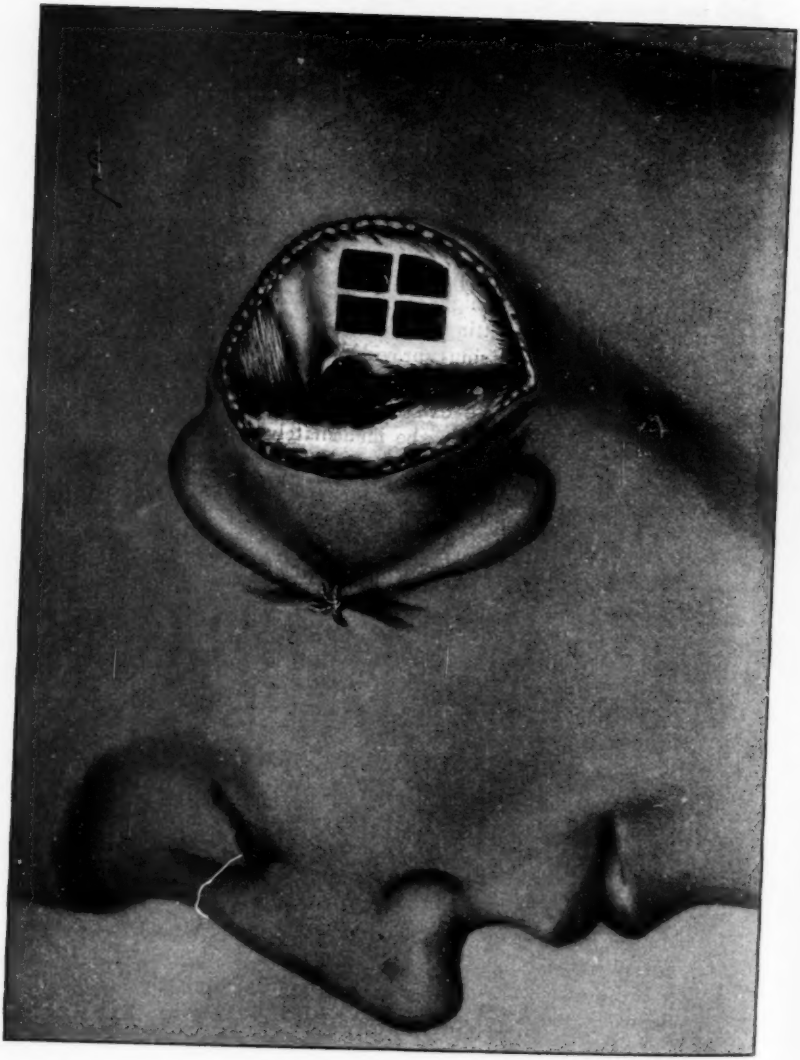
EXPLANATION OF FIG. 2.

Tissues exposed with incision as indicated on Fig. 1, showing tympanic membrane with manubrium of malleus, tympanic plates with auricular process, and suprameatic spine. Behind the meatus the temporal fascia, temporal ridge, mastoid process, mastoid foramen and sternocleidomastoid muscle.



entering the sinus at this point (Fig. 4). This vein is of importance in case of periostitis of the mastoid process, as the inflammation of its walls and its extension inward may be the origin of a thrombus of the lateral sinus; and in cases where the thrombus of the sinus already exists, the blood which is dammed up in the mastoid vein produces œdema of the tissues which it drains, and becomes of diagnostic importance in determining the former condition.

On returning to the description of the middle meatus we find that by severing the tensor tympani muscle in front, and the articular attachment of the incus below, both the malleus and incus can be removed, leaving the stapes *in situ* (Fig. 5). On removal of these two ossicles, the entire inner wall of the meatus can be seen. The upper part, which also forms the inner wall of the atticus, consists of a rounded projection, formed by the horizontal semicircular canal above and a lighter strip below, made up of a thinner plate of bone covering the facial nerve and forming the aqueductus Fallopii. The aqueductus Fallopii extends farther forward than the semicircular canal to the anterior and uppermost angle of the meatus. Below this projection the stapes is seen lodged in the fenestrum ovale, with the stapedius muscle, coming from behind, inserted into its neck. The promontory and fenestrum rotundum forming the lower half of the inner wall are seen to better advantage. The chorda tympani nerve has been removed.

To effect a more thorough and immediate exposure of the entire middle meatus, when radical measures are intended, the removal with a chisel of the tympanic plate as far as the styloid process, in combination with the removal of part of the upper and posterior walls of the external auditory canal, will be found of the greatest advantage as a preliminary step (Fig. 6). By removal of this plate of bone and the superficial lamina of the anterior surface of the mastoid process the entire facial nerve can be exposed and located and followed to the bend in the nerve at the upper anterior angle of the middle meatus. The nerve is lodged at a depth of 2 cm. from the external surface of the mastoid process. Hence, no fear need be entertained of its injury in this part, as it is rarely necessary to penetrate the process to that extent in mastoiditis. But the importance of the anatomical relation of the upper part of the facial nerve (as shown in Figs. 4 and 7) cannot be too strongly emphasized, as its position is such and its protection so slight that in simple operations on the drum or on the contents of the middle ear, or the faulty direction of the chisel in opening the mastoid antrum, the canal may be opened and the nerve injured (abraded,

EXPLANATION OF FIG. 3.

Exposure of middle meatus after removal of tympanic membrane, showing manubrium of malleus, processus longus of incus, promontorium, and fenestrum rotundum. Also pneumatic cells in "mastoid quadrants."

crushed, incised, or severed), thus producing most disagreeable after-effects. The stapes is seen once more lodged in the fenestrum ovale directly below the course of the nerve, but devoid of its muscle on account of removal of its casing of bone posteriorly.

The aditus and antrum (indicated by arrow in Fig. 6) or passage leading from the upper part (atticus) of the middle meatus to the antrum, along which the infection of a middle ear disease so often travels into the antrum, can be shown by removing a sufficient amount of bone from the upper and posterior walls of the bony meatus (Fig. 7). (This is one of the steps in the Stacke-Schwartze "radical operations.") When this is done the plate of bone forming the roof of the tympanic cavity (called the tegmen tympani) is seen; that portion of bone forming the roof of the antrum is called tegmen antri. The tegmen is very thin (½ to 2 mm.) in most skulls and at times incomplete, and can easily be eroded by the acrid discharge of a middle ear disease. This complication often leads to the formation of an extradural abscess of the middle fossa of the skull or to inflammation of its dural lining, which in time may lead to intradural or cerebral abscesses or to inflammation of the entire arachnoid or pia mater.

With the exposure as described, all the necrosed or diseased bone can be removed, which in itself is often sufficient to check an inflammation of the meninges or brain which has been caused by the necrosis.

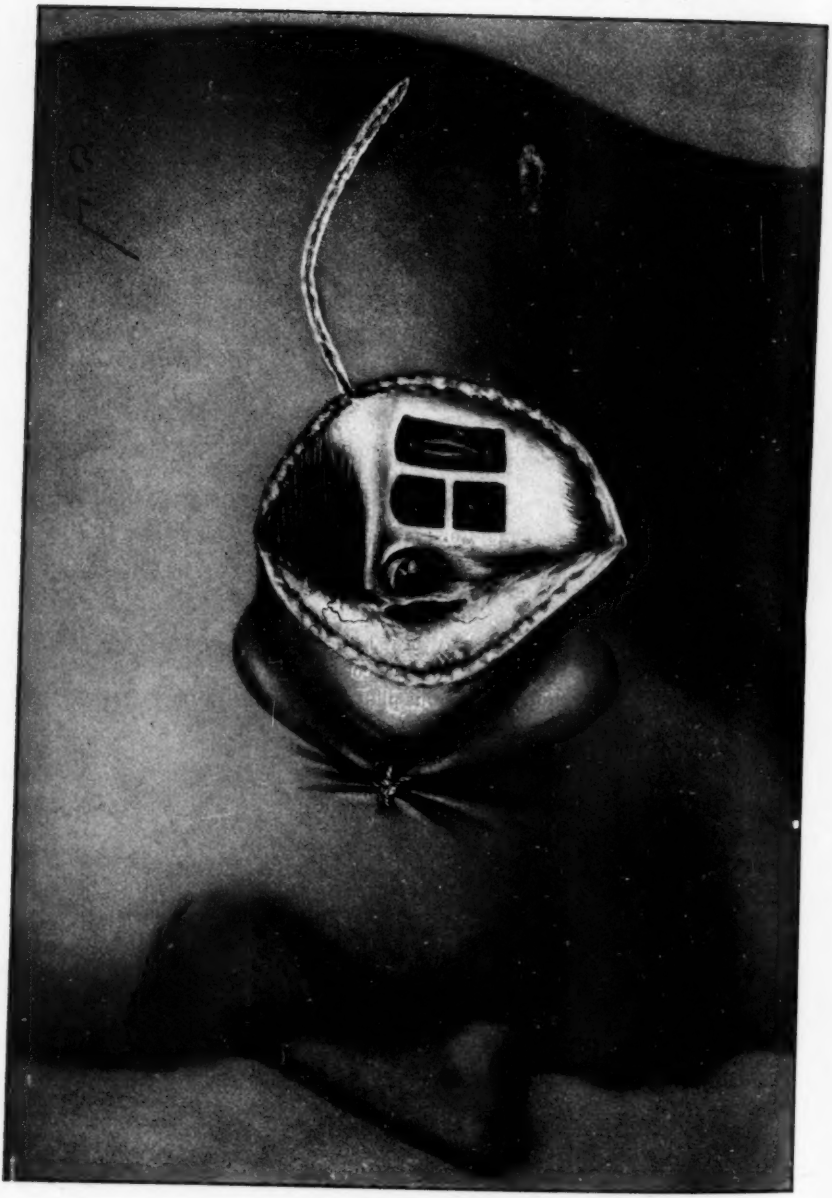
An extradural abscess can be drained through the opening made in the tegmen, while a deep-seated one could be more easily reached through the opening in the squamous plate, as will be mentioned farther on (Figs. 6 and 7).

On removal of the outer wall of the aditus, as mentioned, the projection formed by the horizontal semicircular canal is seen forming a part of the floor and inner wall of the aditus (Fig. 7). It will be readily understood how easily the canal can be opened if on exposing the antrum the chisel is directed too far forward or downward at a depth greater than 1½ cm.

On dislodging the facial nerve from its groove, the inner wall of the aqueductus Fallopii is shown extending from the upper anterior angle of the middle meatus backward directly below the horizontal semicircular canal, with the fenestrum ovale beneath it; it then bends downward, with the fenestrum rotundum in front of it, and reaches the stylomastoid foramen at a depth of about 1½ cm. from the outer surface of the mastoid process.

EXPLANATION OF FIG. 4.

Portion of upper and posterior walls of external bony meatus removed, showing tensor tympani muscle attached to malleus anteriorly; chorda tympani nerve emerging from aqueductus Fallopii, posteriorly, crossing incus; below this the stapedius muscle, promontorium and fenestrum rotundum. The upper anterior quadrant shows the mastoid antrum; the upper posterior, the lateral sinus with mastoid vein; the two lower quadrants, mastoid cells.



On removal of the tympanic plate the floor of the tympanic cavity is seen to consist of bone varying in thickness from ¼ to ½ cm. Frequently this helps to form the outer wall of the jugular fossa, and where necrosis of the bone or inflammation of the communicating veins in the bone has taken place, an inflammation or thrombosis of the bulbar portion of the jugular vein, which is contained in the fossa, results.

Continuing with the dissection of the mastoid process, we find that on removing the ledge between the upper and lower posterior windows (as shown in Fig. 5) and making them continuous, a longer stretch of the descending limb of the sigmoid flexure of the lateral sinus can be exposed, and its walls more readily incised, if it is necessary to inspect its interior or to determine its contents. By inspecting its interior you can determine if an adhering thrombus exists which does not clog the entire lumen. Incomplete thrombi are more frequent where the sinus enters the jugular vein in a more or less straight line, while if they join at an acute angle the thrombus is more often complete. A coating or granulations on the outer side of the sinus, or necrotic areas in its wall, make the presence of a thrombus probable. If no clot is present in such a case, the opening must be packed with gauze and equable pressure made, by means of a graduated conical compress, to control the hemorrhage. If the inner wall is to be inspected, the hemorrhage must be controlled by packing or compressing the sinus at both ends. If a clot is found, this must be removed and the ensuing hemorrhage controlled as just mentioned. If the entire removal of the clot is not successful, an extended incision must be made above or below or in both directions, according to the extension of the clot, so that complete patency of its lumen is established and the entire sinus can be inspected for possible necrosis of its wall.

The entire course of the sinus can be exposed above by an incision commencing at the upper posterior quadrant in a direction upward and backward and then gradually downward until it reaches the external occipital protuberance, which corresponds on the inside of the skull to the torcular Herophili (Fig. 5). The bone covering it can be removed by means of a chisel, circular saw, or drill, and the dural covering incised along its entire course, if this should be found necessary in order to remove the clot or infected matter filling the canal, or to excise the wall itself if found necrotic (Fig. 6).

EXPLANATION OF FIG. 5.

The malleus, incus, and chorda tympani nerve removed from middle meatus, showing projection formed by external semicircular canal and aqueductus Fallopii, stapes in fenestrum ovale with stapedius muscle attached posteriorly. Ledge removed between posterior quadrants exposing descending limb of lateral sinus (sigmoid flexure), which is incised. Incision from upper posterior quadrant backward for exposure of horizontal limb of lateral sinus.

About 1 cm. above the posterior window the slit leading to the superior petrosal sinus can be seen. Posteriorly the opening to the sinus of the other side is visible, and somewhat in front and above this the longitudinal sinus has its termination. Along the entire course of the lateral sinus, slits representing the entrance of cerebral veins can be seen. Frequently fibrous bands are also found stretching across the lumen and forming supports to maintain the patency of the canal against the pressure exerted by the weight of the brain.

Below and in front, corresponding to the lower posterior window, the sinus will be seen to dip in toward the jugular fossa, forming the lower limb of the sigmoid flexure.

If the symptoms and physical signs of the case make probable the presence of an extradural, intradural, or cerebral abscess, especially of the temporal lobe, which occurs more frequently, or the presence of fluid in the ventricles, a puncture of the brain in various directions can be made through a trephine opening in the squamous portion of the temporal bone. This can be readily exposed on retracting the temporal muscle upward after removal of its fascia (as shown in Figs. 5 and 6). On removing the button of bone, a branch of the middle meningeal artery is frequently seen traversing the space. A long aspirating needle or narrow-bladed knife can be passed into the brain in various directions until the presence or absence of pus in the brain or excessive accumulation of cerebro-spinal fluid in the ventricles is determined and located. If pus is found and the trephine opening is not of sufficient size to afford proper drainage, the temporal muscle can be still further detached and all the soft parts be retracted upward and forward so that the opening can be enlarged in various directions.

If the diagnosis of abscess is positive beforehand, and the cerebral cavity is to be opened in combination with the radical ear operation, a quadrilateral osteoplastic flap is made of the squamous portion of the temporal bone and turned forward as mentioned farther on.

If on incising the lateral sinus in the upper posterior window (as shown in Fig. 7) a suspected sinus affection is not found to exist, but the train of symptoms points to the presence of a serious complication in this region, the dura of the cerebral or cerebellar lobes can be exposed by a single or double "trap-door" incision, the course of the lateral sinus serving as a median line from which the osteoplastic flaps can be cut above and below. The incision in the dura mater

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EXPLANATION OF FIG. 6.

Outer wall of aqueductus Fallopii and the tympanic plate has been removed, exposing the facial nerve. Arrow in aditus ad antrum. Interior of entire lateral sinus exposed, showing slit for superior petrosal sinus anteriorly and openings for longitudinal and right lateral sinus posteriorly. Trephine opening in squamous plate, with middle meningeal artery showing.

should be made on three sides only, and should leave a sufficient margin to which the flap can be sewed when replaced subsequently.

Through this exposure the occipital convolutions of the cerebrum, the entire half of the tentorium cerebelli, and the posterior fossa of the skull, with its cerebellum, can be inspected, and extradural, intradural, or brain abscesses can be incised and drained. A simple and tolerably accurate method of locating the horizontal limb of the lateral sinus, without the aid of the mastoid quadrants, is Chipault's method, which consists in taking a point 95 per cent. of the distance between the nasion and inion and joining it by a straight line with the retro-orbital tubercle. The posterior half represents the course of the horizontal limb of the sinus (see sketch under technique, below).

To afford a sufficient exposure for a very deep dissection of the petrous portion of the temporal bone, it is necessary to remove a plate of bone from above the ear, preferably quadrilateral in shape, about 4 cm. long and 3 cm. wide, to include the portion of the squamous plate lying over the posterior half of the zygomatic arch, and reaching back as far as the middle of the mastoid process. The flap, containing skin, muscle, and bone, and nourished by a branch of the temporal artery, is turned forward (Fig. 8).

By retracting the dura from the upper surface of the petrous bone, resistance will be met with in front, where the middle meningeal artery emerges from the foramen spinosum. At a depth of about 3 cm. from the exterior of the skull the carotid artery can be exposed on removal of its bony canal from above. The cochlea will be found situated in the angle formed by the artery as it bends inward and forward from below, while the Eustachian tube, with its gallery containing the tensor tympani muscle, hugs it anteriorly (Fig. 11). The opening of the Eustachian tube in the upper anterior angle of the middle meatus is directly in front and external to the ascending limb of the artery. In cases where but a thin layer of bone covers the artery, or where the bone is entirely absent in this situation, the artery can be seen pulsating on examining the middle ear, and its puncture by a paracentesis needle carried too deeply is possible. Here, too, necrosis of the inner wall of the tympanic cavity, forming the bony canal of the artery, can produce a destructive process in the wall of the vessel and cause fatal hemorrhage if not ligated below in time. The artery is at a depth of about 2 cm. from the auditory process, and

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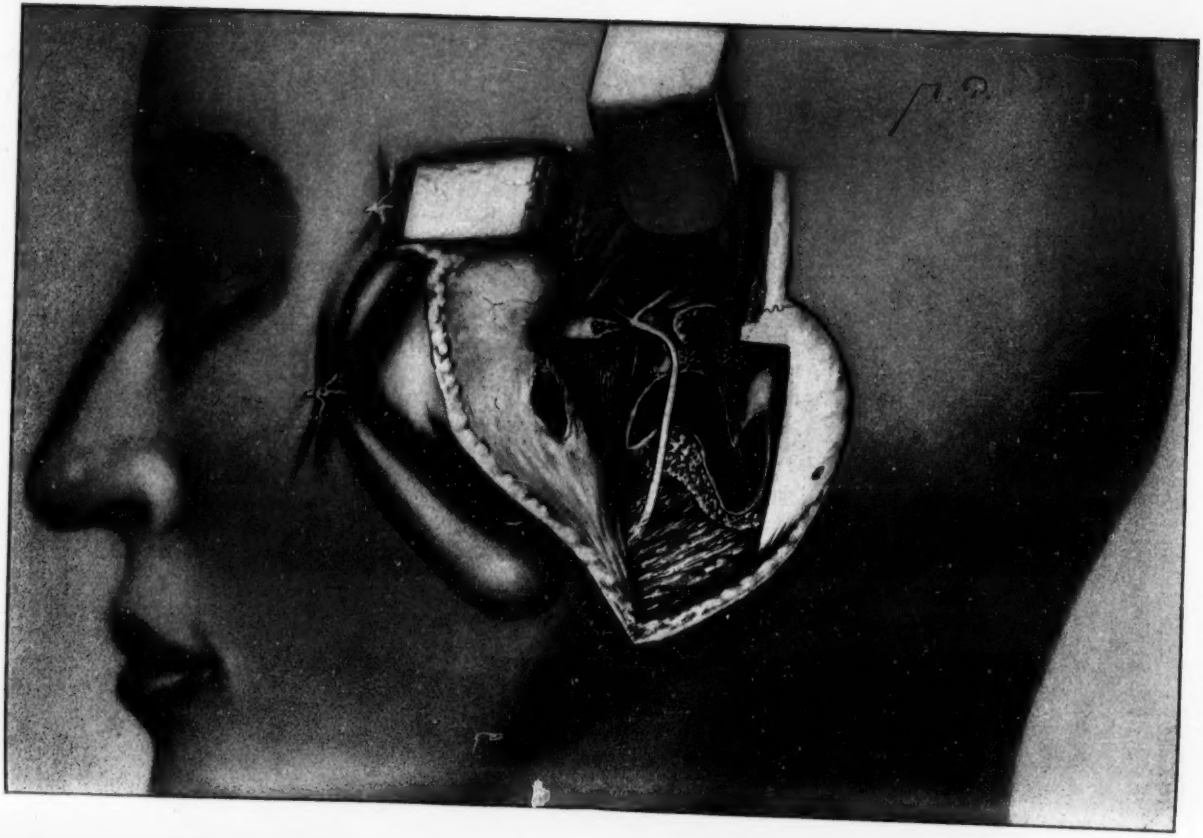
EXPLANATION OF FIG. 7.

Bone of external meatus and outer wall of aditus ad antrum chiselled away, exposing the tegmen tympani, tegmen antri, atticus, aditus ad antrum, mastoid antrum, and external semicircular canal. The facial nerve is dislodged from the aqueductus Fallopii, and the fenestra ovale and rotundum appear below. Posteriorly two osteoplastic flaps, with horizontal limb of lateral sinus chosen as median line for exposing cerebral and cerebellar convolutions.



has the jugular vein directly behind it and somewhat to its outer side. In all the previous dissections the facial nerve has been exposed only from the anterior superior angle of the middle meatus. If we follow the course of the nerve in the aqueductus Fallopii as it emerges from the internal auditory meatus and passes forward between the cochlea and vestibule, it forms an angle of 45° with the long axis of the skull (Figs 8 and 11). As it enters the middle meatus it turns outward and backward, forming an elbow from the point of which the superficial petrosal nerve is given off. The latter passes inward and forward through the hiatus Fallopii along the upper surface of the petrous bone until it reaches the middle lacerated foramen.

The base of the cochlea is formed by the anterior wall of the internal auditory meatus; its apex juts against the Eustachian tube. To its inner side is the carotid canal; to its outer the aqueductus Fallopii, with the facial nerve above and the vestibule below.

The vestibule is seen at the outer side of the facial canal with the horizontal semicircular canal coming from it externally, and the perpendicular semicircular canal superiorly.

The exposure of the sigmoid flexure of the lateral sinus has been brought about by the removal of almost the entire mastoid process (Fig. 8). In this procedure injury to the facial nerve must be avoided. This nerve emerges from the stylomastoid foramen, at the depth of about 1½ cm. from the anterior border of the process, and when located the nerve should be gently drawn forward, as the jugular vein will be found ½ cm. to its inner side. The nerves accompanying the sinus through the posterior lacerated foramen are covered by it so that they need not be considered. The foramen magnum lies 1½ cm. to its inner side and posteriorly. When the sinus is opened, slits of the inferior petrosal and occipital sinuses and the condyloid vein can be seen where these vessels enter the jugular vein. The jugular fossa, which contains the bulb of the vein, varies in shape in different skulls and on both sides of the same skull. At times it is vaulted and smooth and approximates the floor of the middle meatus, but it may be low, contracted, and traversed with irregular ridges. The former condition is considered a predisposing cause in thrombosis of the bulb of the jugular vein on account of the more intimate relation of this part with the

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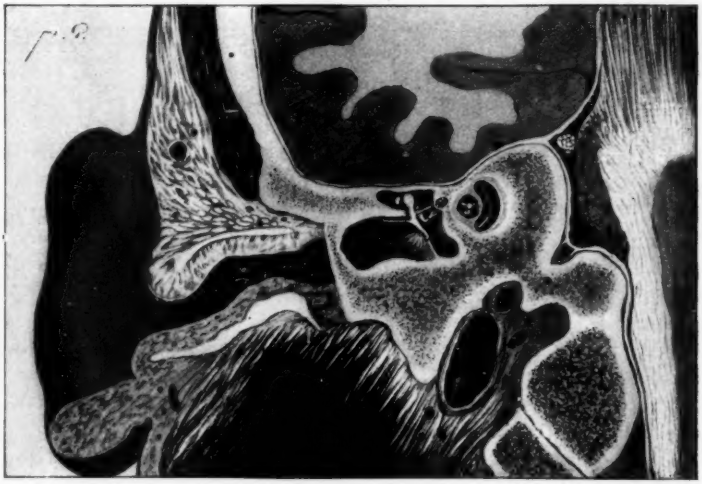
EXPLANATION OF FIG. 8.

Deep dissection of temporal bone, with osteoplastic flap of squamous plate, exposing dura mater, carotid artery, entire course of facial nerve in temporal bone, giving off the superior petrosal nerve at its bend above the middle meatus; turns of the cochlea between the facial nerve and carotid artery above, and the vestibule with superior and exterior semicircular canals, and antrum, posteriorly. The remaining portion of inner wall of middle meatus shows opening of Eustachian tube in front and fenestra ovale and rotundum behind. Below these the sigmoid flexure of the lateral sinus is seen in the openings of the posterior condyloid vein and inferior petrosal sinus.



EXPLANATION OF FIG. 9.

Cross-section of right side of head, showing external meatus, separated from middle meatus by outer wall of atticus above and tympani muscle below. On the middle meatus are seen the tegmen tympani, the ossicles, the tensor tympani muscle, and projections of the aqueductus Fallopii, with facial nerve above and first turn of cochlea below. Deep in the bone the cochlea. Below, the bulb of the jugular vein.

EXPLANATION OF FIG. 10.

Cross-section of left side of head, 1 cm. behind previous section. A small portion of the posterior wall of external meatus is seen. Internal to this, the tegmen, aditus ad antrum, projections of external semicircular canal and posterior wall of middle meatus. The vestibule shows bristles coming from the superior and external semicircular canal. The internal meatus contains the facial and auditory nerves. Below is seen the jugular vein with openings of the posterior condyloid vein and inferior petrosal sinus.

middle meatus; and the same is also claimed, on account of the more tortuous course the blood stream is subjected to. Infectious material might pass along the entire route of the sinus without producing any harm, but at the jugular fossa the flow of venous blood is checked, producing currents (whirlpool) which favor the formation of a thrombus, on account of the greater liability to injury and infection which the wall of the vein is subjected to.

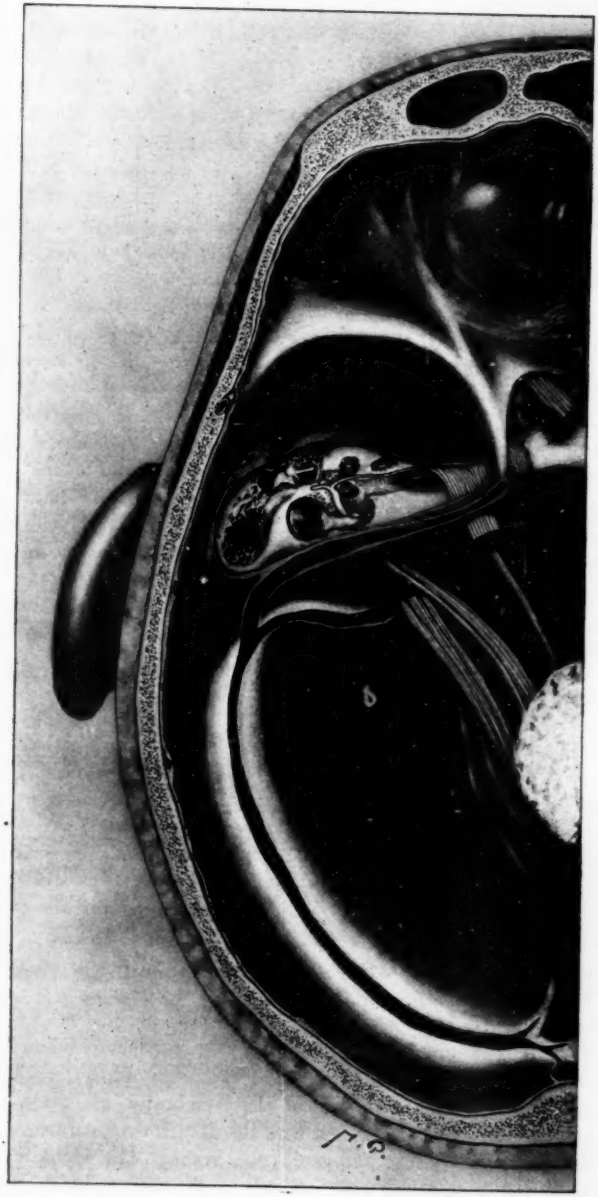
If the bulb of the vein alone is involved, the jugular should be ligated before the sinus and bulb are incised; but if the infection has gone farther, and a cord-like strand on the side of the neck indicates an extensive thrombus of the vein, ligation should not be performed.

To demonstrate the intimate relation between the ear and the cerebral cavity, a transverse section of the head through the centre of the middle meatus has been made (Fig. 9). The external auditory canal is seen slanting upward and inward, its outer half lined with short hairs directed outward. The external is separated from the middle meatus above by a plate of bone which forms the outer wall of the atticus, while below is the tympanic membrane, with the manubrium and processus brevis of the malleus attached to it. The roof of the middle meatus has a thin plate of bone, the tegmen tympani, separating it from the cerebral cavity.

A section of this kind demonstrates the intimate relation between the two parts and shows how readily an erosion or a fissure in the division line may lead to serious involvement of the brain and its covering when the middle ear is inflamed.

On the inner wall of the meatus can be seen, from above downward, first, the projection made by the aqueductus Fallopii with its facial nerve; underneath this the tendon of the tensor tympani muscle emerging from the upper part of the Eustachian tube. Directly behind it and on the same level is the fenestrum ovale, containing the stapes. From here on downward the promontorium, representing the beginning of the cochlea, bulges outward, forming a recess with the floor of the meatus. The floor consists of a varied thickness of bone and occasionally communicates with the jugular fossa through fissures or small lymph channels.

The cavity of the meatus contains the ossicles. Of these the malleus is anterior, with its head in the atticus, the tendon of the tensor tympani muscle attached to its neck, and the suspensory ligament extending from the tegmen to its head. Its short process projects outward, throwing the upper part of the membrane into folds, and the manubrium extends downward, with its tip turned outward, attached to the mid-point of the tympanic membrane. The incus is located posterior to the malleus, with its body in the atticus, its short process in the aditus, and its long process projecting downward and articulating



with the head of the stapes. The stapes is lodged in the fenestrum ovale, with the stapedius muscle attached to its neck posteriorly, and lies horizontally and at right angles both to the malleus and incus.

Internal to the middle ear and set in the most compact part of the petrous bone are the spiral turns of the cochlea, with the apex pointing out and forward and the base butting against the wall of the internal auditory meatus.

Below the bony framework surrounding the ear and lying somewhat to the inner side of the middle meatus is the bulb of the jugular vein, in the jugular fossa.

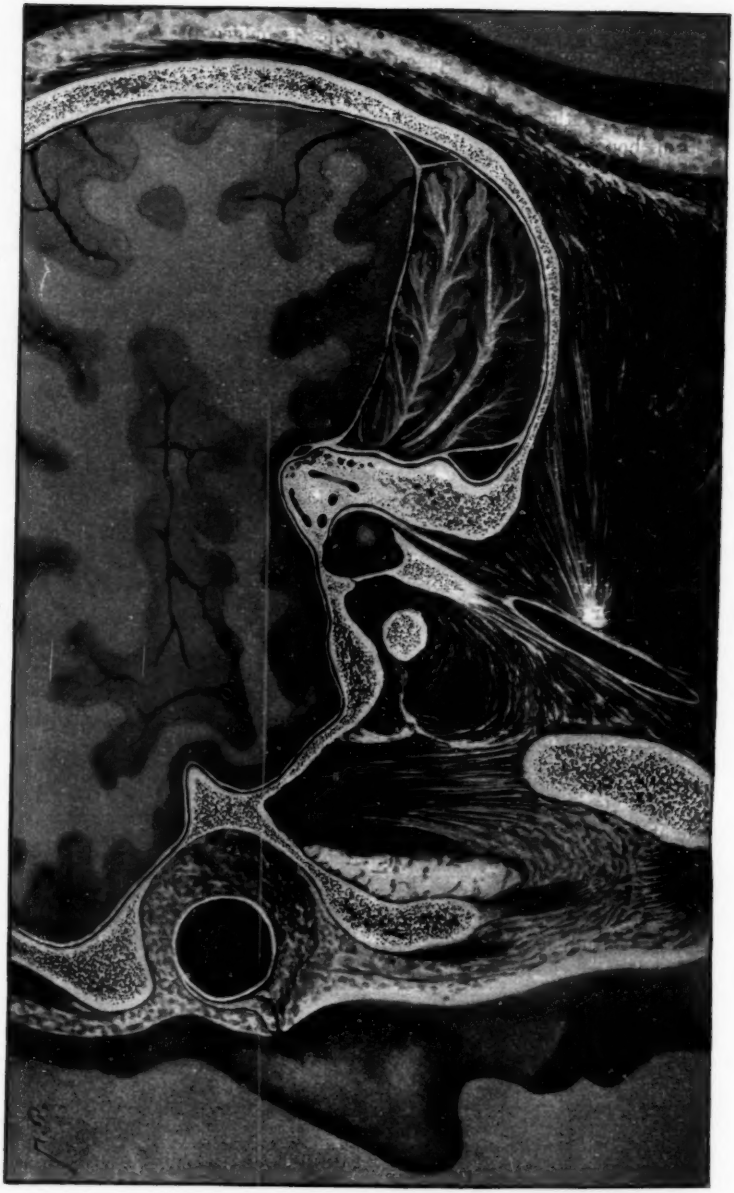
A transverse section of the head, about 1 cm. behind the one just described (Fig. 10), shows only a small portion of the posterior wall of the external meatus, and parts of the middle and inner meatus corresponding to that level. Above, a thin plate of bone is seen separating the cerebral cavity from the aditus ad antrum. The aditus, shaped like an inverted pyramid, has the protrusion of the horizontal semicircular canal forming a part of its floor and inner wall. Below this is seen the posterior wall of the middle meatus proper, made up of irregular, open bony cells covered with a delicate mucous membrane, which lines the meatus and communicating cavities. Internal to these parts can be seen the interior of the vestibule, with the openings of the semicircular canals on its outer side. Anteriorly, the anterior ends of the superior or vertical and the external or horizontal canals have a common opening, while posteriorly the posterior end of the superior and the upper end of the posterior canals have a common opening. The openings of a horizontal canal lie on the same plane, while those of the posterior canal lie one above and the other below the posterior opening of the horizontal canal (Fig. 12).

The exterior of the superior or vertical semicircular canal forms a slight protuberance on the upper surface of the petrous bone corresponding to its course, from in front and externally, back and internally.

Internal to the vestibule is the internal auditory meatus containing the facial and auditory nerves; the facial above, directed toward the aqueductus Fallopii, and the auditory below, about to enter the vestibule and cochlea.

EXPLANATION OF FIG. 11.

The dura mater of the middle fossa of skull is cut away, showing a dissection of the temporal bone. From without inward are seen the mastoid antrum behind, the middle meatus with ossicles in front, and the aditus ad antrum between. The vestibule shows the openings of the semicircular canals. The facial nerve has the superior petrosal nerve coming from its bend and passing inward. In front of the nerve the tensor tympani muscle is seen in the Eustachian tube; behind it, the cochlea and internal auditory meatus. Internal to these the carotid canal, the carotid artery, and the Gasserian ganglion. Posteriorly the lateral and superior petrosal sinus have been slit open. The seventh and eighth nerves are seen entering the internal auditory meatus; the ninth, tenth, and eleventh the jugular fossa.



The bulb of the jugular vein is seen in the fossa, and several slits indicate the entrance of emissary veins.

On inspecting the middle and posterior fossa of the skull, when the brain has been raised from its bed, and removing the dura mater over the petrous bone in the middle fossa, the following structures can be exposed by chiselling the bone (Fig. 11): Externally, the mastoid antrum; in front of it, and coming from the middle meatus, the aditus ad antrum. The horizontal semicircular canal is seen helping to form the inner wall and floor of this passage. The middle meatus is anterior and internal to the antrum, and presents the malleus and incus in the atticus, and the tympanic membrane deep down, forming its outer wall. The tensor tympani muscle is seen in its groove in the upper part of the Eustachian tube, passing outward and backward, and becoming inserted into the neck of the malleus. The facial nerve is seen as it disappears at the upper anterior angle of the middle meatus, forming an elbow from the angle of which the superior petrosal nerve is given off. Posterior to this point it lies between the cochlea, which is on its inner and the vestibule, which is on its outer side. In the internal auditory meatus it lies above the auditory nerve, and in the posterior fossa to its outer side.

The vestibule shows the groove of the superior semicircular canal and the openings of the other two canals. The cochlea lies in the back part of an angular recess formed by the bend in the carotid canal as it ascends from the base of the skull, and has the tympanic cavity and aqueductus Fallopii, with the facial nerve to its outer side. The Eustachian tube is in front, the internal auditory meatus behind, and the compact bone over the carotid canal to its inner side.

The carotid canal has the general direction of the petrous bone inward and forward, with the Eustachian tube immediately in front of it, the superficial petrosal nerve coursing over it as it passes from the hiatus Fallopii to the middle lacerated foramen and compact bone behind it. As it ascends from the base of the skull it is directly internal to the inner wall of the middle meatus. As the canal passes inward toward the middle lacerated foramen, the Gasserian ganglion lies over it, in a depression at the inner end of the superior surface of the petrous bone.

The middle meningeal artery can be seen through the dura mater as it emerges from the foramen spinosum, and sends its anterior and

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EXPLANATION OF FIG. 12.

Anterior-posterior section through middle meatus. On inner wall of middle meatus are seen the opening in processus cochleariformis and Eustachian tube in front; facial nerve behind, and fenestrum ovale and rotundum, with promontorium below. Above the middle meatus are seen the superior, external, and posterior semicircular canal and superior petrosal sinus. Below are the styloid process, stylomastoid foramen, and jugular vein. Also cerebrum, tentorium cerebelli, cerebellum, and lateral sinus.

posterior branches outward and upward, grooving the skull in its course. The superior petrosal sinus is seen running along the superior posterior border of the petrous bone, joining the lateral with the cavernous sinus.

The lateral sinus extends from the torcular Herophili behind to the jugular foramen in front. At the torcular it communicates with the lateral sinus of the other side, the longitudinal sinus above, and the occipital below. The part which descends from the horizontal limb to the jugular foramen is known as the sigmoid flexure of the lateral sinus. It forms an elbow with the horizontal limb, and passes downward and inward in the deeply grooved bone until it reaches the posterior lacerated foramen, where it is joined by the inferior petrosal sinus and the posterior condyloid vein to form the internal jugular vein. It is accompanied by the ninth, tenth, and eleventh nerves.

If a vertical antero-posterior section of the head is made to pass directly through the tympanic cavity (as seen in Fig. 12) the following points of interest can be shown: Between the tympanic and cerebral cavities the tegmen tympani, on the inner wall of the middle meatus, which is covered by delicate mucous membrane, the orifice of the Eustachian tube and the canal for the tensor tympani muscle (processus cochleari formis); the latter has an orifice at its posterior end, and transmits the tendon of the tensor tympani muscle; behind this the aqueductus Fallopii, with the facial nerve passing back and down, around the fenestrum ovale; underneath this the promontorium, with the fenestrum rotundum. Projecting from the floor downward is the styloid process. Below this is a section of the jugular vein.

Above and posterior to the middle meatus is the body of the petrous bone traversed by the semicircular canals. The openings of the horizontal or external one are above and parallel to the facial nerve; the vertical or superior passes from in front upward and posteriorly; the posterior canal is situated behind, with one opening above and the other below the posterior opening of the horizontal, as mentioned previously.

At the upper posterior border of the petrous bone is the superior petrosal sinus. A part of the sigmoid flexure of the lateral sinus is seen at a point where the occipital meets the petrous bone. The opening of the lateral sinus is seen behind at a point where the tentorium cerebelli meets the dural lining of the occipital bone. The tentorium is seen separating cerebral from cerebellar convolutions.

In recapitulating the operative technique mentioned in the foregoing pages five separate procedures may be described:

First, "radical" exposure of the middle ear; second, exposure of the mastoid antrum; third, exposure of the mastoid antrum and cells and lateral sinus ("mastoid quadrants"); fourth, exposure of the

temporal lobe of the brain and middle fossa of the skull; fifth, exposure of the occipital lobe of the brain, tentorium cerebelli, cerebellum, and posterior fossa of the skull.

For the "radical" exposure of the middle ear an incision is made ½ to 1 cm. behind the attachment of the auricle extending from above the ear downward to the tip of the mastoid process (Fig. 1). Above the temporal ridge, which corresponds in height to the upper wall of the outer meatus (Fig. 2), the incision should be through skin and superficial fascia alone, leaving the temporal muscle intact. Below the ridge it should pass directly to the bone. The tissues are dissected forward and the periosteum elevated until the bony meatus is reached. To avoid possible necrosis of the tympanic plate the soft parts of the posterior and upper wall of the soft meatus alone should first be detached with an elevator and then incised by means of a thin-bladed knife near the tympanic membrane and held against the anterior wall with a long, narrow retractor; or, if the tympanic plate is to be chiselled away, the anterior and lower walls can be cut also and the entire funnel of soft tissues drawn out of the bony canal and retracted with the auricle. The tympanic membrane is now cut from its ring of bone and removed with the malleus after the attachment of the tensor tympani muscle has been severed. With a chisel, or preferably a burr drill, the outer wall of the attic, which corresponds to the inner part of the upper wall of the external meatus, is then removed until the roof of the attic is continuous with the upper wall of the external meatus (Figs. 4 and 5). If this does not give a sufficient exposure the tympanic plate can be chiselled away as far as the styloid process (Fig. 6). After removal of the incus (Fig. 5), which should be cautiously done, so as not to dislodge the stapes from the fenestrum ovale, a probe should be passed through the aditus into the antrum, and the bone chiselled or drilled away external to it (Figs. 6 and 7). The interior of the cavities are now curetted and smoothed, care being taken not to open the aqueductus Fallopii and horizontal semicircular canal, nor to dislodge the stapes. If the tegmen is necrosed, this should be removed, but puncture of the dura mater should be avoided. An extradural, intradural, or cerebral abscess can be located or drained through this aperture, but a trephine opening through the squamous plate of the temporal bone, after the temporal muscle has been detached and drawn upward, is better for this purpose (Fig. 6). The latter will also suffice for aspirating the lateral ventricles for excessive accumulation of cerebro-spinal fluid. If a deep dissection of the temporal bone is necessary, especially if the upper surface of the petrous bone is to be exposed, or if an abscess is not drained sufficiently through the trephine opening just mentioned, a quadrilateral osteoplastic flap, 3 cm. wide and 4 cm. long, with its base anteriorly, should

be made to include the portion of squamous bone lying over the posterior half of the zygomatic arch, and reaching back as far as the middle of the mastoid process (Fig. 8). If the upper portion of the petrous bone is to be chiselled, the dura mater should be elevated gently and the brain retracted with a broad, blunt retractor. More room can be obtained by incising the dura and permitting some cerebro-spinal fluid to escape. This should not be done if pus is present or if the brain or its coverings have not already been attacked. After the tissues have been replaced to their original position and sutured, an opening is left sufficiently large for drainage, and the wound packed with gauze until epidermization of the exposed parts is complete.

To expose the mastoid antrum an incision is made ½ to 1 cm. behind the auricle, extending from a point corresponding in height to the upper wall of the external meatus downward to the tip of the mastoid process (see cross on Fig. 1). The tissues are dissected forward and the periosteum elevated until the suprameatic spine can be felt with the finger or an instrument. Keeping below the temporal crest, an opening is made with a chisel or burr drill 1 cm. behind the suprameatic spine. The instrument should be directed forward, inward, and slightly upward, corresponding to the direction of the external meatus to a depth of 1 to 2 cm. When the instrument has penetrated deeper than 1½ cm., care must be taken not to open the horizontal semicircular canal or aqueductus Fallopii. When the antrum has been reached, granulations or irregular bony ridges should be removed by means of a curette, care being taken to avoid piercing the tegmen antri above or the bone behind which separates the antrum from the lateral sinus. If the latter be exposed no harm need necessarily result, but if punctured, the hemorrhage must be controlled by packing the bony wound with a graduated gauze tampon. When the antrum is clean and smooth the parts are replaced and sutured, leaving an opening for drainage. When the cavity is again in a healthy condition the opening will close by granulation, or a small plastic operation will be required to effect this.

If the lateral sinus is to be exposed with the antrum and mastoid cells, the mastoid process should be divided into four quadrants, as described previously (Figs. 3 and 4). The anterior superior quadrant is opened first with the instrument directed as mentioned in the previous operation, and the antrum cleaned and packed. Next, the two lower quadrants should be opened and evacuated. After packing these to prevent inflammatory discharges from spreading, the upper posterior quadrant should be entered and the lateral sinus exposed. Here the instrument, preferably a burr drill, should be directed straight in. Palpation of the sinus must be performed very carefully, in order not to dislodge adherent or incomplete thrombi. In such a case, aspira-

tion with a hypodermic syringe might show blood and lead to an erroneous diagnosis, so that an exploratory incision is safer. For this purpose the lower posterior quadrant should be drilled sufficiently deep to expose the sinus below, and the ledge between the upper and lower quadrants should be removed in order to make them continuous.

To expose the entire sigmoid flexure of the lateral sinus and the bulb of the jugular vein, the lower portion of the mastoid process must be removed (Fig. 8). The facial nerve should be located and exposed to its exit at the stylomastoid foramen, and the spongy bone between it and the sinus chiselled away. Posteriorly the foramen magnum must be avoided. If the thrombus is still confined to the upper portion of the jugular vein, ligation should be performed below this point before the sinus is incised.

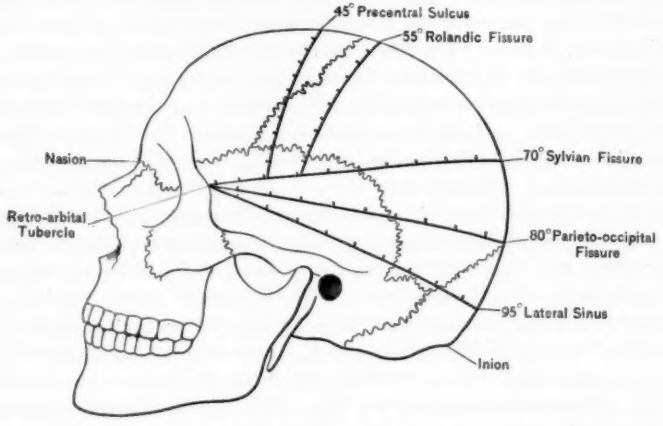
If the horizontal limb of the sinus is to be exposed, an incision from the upper posterior quadrant, first upward and backward, and then downward and backward toward the external occipital protuberance, is to be made (Figs. 5 and 6). A strip of bone is then removed by means of a chisel, circular saw, or drill, and the sinus incised to the extent of the clot. Hemorrhage is to be controlled with gauze strips or compresses, the former to be introduced directly into the lumen; or, if this is insufficient, compression should be applied to the external surface of the sinus after detaching it from its bony casing. The parts are subsequently replaced and sutured, a sufficient opening being left for drainage.

To expose the occipital lobe of the brain, the cerebellum, or posterior fossa of the skull, a single or double "trap-door" incision is made above and below the lateral sinus (Fig. 7). To locate the latter, Chipault's method can be applied. It consists in taking 95 per cent. of the distance between the nasion and inion, and joining this point with the retro-orbital tubercle. The posterior half of the line represents the horizontal limb of the lateral sinus.

The incision through the bone is made by means of a circular saw, a drill, or Gigli's wire saw, and trephined. The base of the bony flap is to be nicked on either side with the chisel, so that the bone will break off in a straight line when pried open with the elevator. The dura is to be incised in the same direction as the outer flap, a sufficient margin being left if the condition found permits subsequent suturing.

Other points of interest in cranial topography are located by the same method just mentioned (Chipault's), to wit: A point 80 per cent. of the distance between the nasion and inion joined with the retro-orbital tubercle represents the course of the parieto-occipital fissure. A point 70 per cent. the distance of the same sagittal line joined with the tubercle represents the course of the fissure of Sylvius. If the latter be divided into tenths, and the junction of the third and fourth tenth be

joined with the 55 per cent. point on the longitudinal line, the course of the Rolandic fissure is shown; and if the junction of the second and third tenth on the Sylvian line be joined with the 45 per cent., the precentral fissure is indicated. The middle meningeal artery crosses between the second and third tenths of the three primary lines.



In conclusion, I wish to express my indebtedness to Professor Frank Hartley for the many valuable suggestions offered during the progress of this work. I also wish to acknowledge the painstaking efforts of Mr. M. Peterson, draughtsman for the anatomical department, in producing anatomical accuracy in the accompanying drawings.

GANGRENOUS CHOLECYSTITIS, WITH A REPORT OF A CASE IN WHICH A SUCCESSFUL CHOLECYSTECTOMY WAS DONE.

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Gangrenous cholecystitis is a pathological condition sufficiently rare to warrant the report of every case. It may be looked upon as an extreme degree of phlegmonous cholecystitis, which is more frequently met with, but this condition usually results in death before a true gangrene of the gall-bladder is established. Robson, in the second edition of his book on *Diseases of the Gall-bladder and Bile Ducts*, speaks of gangrenous cholecystitis as "extremely rare," and says that he has been able to find but one case reported, that of Hotchkiss

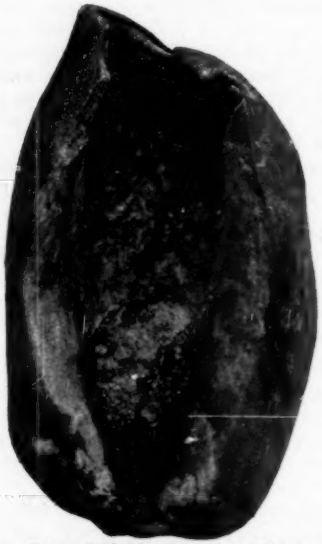
(*Annals of Surgery*, February, 1894). Robson, however, reports a case of his own which might be classed under this head. In the second edition of Kehr's book can be found no mention of a case of gangrenous cholecystitis. Mayo, however, has reported one case in which the gall-bladder was successfully removed. Including Mayo's second series (*Annals of Surgery*, June, 1902), in which no such case is reported, it may be stated that there was only one case in 433 operations upon the gall-bladder and ducts, performed by W. J. and C. H. Mayo. These statements show the great rarity of a true gangrenous cholecystitis. Before discussing the condition I will briefly report a case in which the gall-bladder was successfully removed.

The patient, a woman, aged fifty-two years, was admitted to the Polyclinic Hospital on October 3, 1902. There was nothing in her previous history worthy of note excepting that she had suffered from frequent attacks of indigestion accompanied by nausea and vomiting. During these attacks she had been able to retain practically no food. The pain had never radiated to the shoulders, nor had the patient ever been jaundiced.

Her present illness began three days before admission, with pain in the left hypochondriac region and vomiting. These symptoms kept up intermittently. I saw the patient on the evening of October 3d. At this time she had a temperature of 102° F., pulse of 112, and respiration of 32. She complained of pain and tenderness on the right side of the abdomen, but these were less severe than they had been; the bowels were constipated. There was considerable rigidity of the abdominal muscles on the right side, and a tumor was palpable, which was smooth and which seemed to move away from the examining hand. I was asked to see the case as probably one of appendicitis, but the position and condition of the tumor convinced me that the case was not one of appendicitis. The next morning the leucocyte count was 37,600. At this time there was more tenderness and more rigidity; so much more in fact that the tumor could not be palpated. Immediate operation was determined upon.

When the patient was anæsthetized and the abdominal muscles relaxed it was easy to diagnose a distended gall-bladder. An incision was made over the tumor, and when the abdominal cavity was opened some free fluid was found. The gall-bladder was covered by an adherent omentum, which, when removed, showed the organ to be distended and its entire fundus of a dark purple color. A number of large abdominal pads were inserted, the gall-bladder incised, and a quantity of very foul pus evacuated. The mucous membrane was green and gangrenous throughout. A large stone was found fixed at the mouth of the cystic duct. The whole fundus of the gall-bladder was gangrenous through all its coats. The line of demarcation between this and the remaining portion of the gall-bladder was very clear. This portion was quite thin, but the rest of the organ was very much thickened, measuring from one-half to one inch, as is shown in the accompanying photograph. It was decided to remove the gall-bladder, and its separation from the liver was easily accomplished by means of the finger, the tissues being soft from infil-

tration; no bleeding resulted from this separation. When an attempt was made to pass a ligature about the cystic duct the gall-bladder separated and came away. This took place when very little traction was being made upon it before the first knot in the ligature was tied, which well illustrates the condition of the organ even as low down as the cystic duct. The cystic artery bled freely and could not be controlled by a hæmostat, as the instrument cut through the inflamed tissues. Gauze packing was then introduced and controlled the hemorrhage absolutely. A number of large gauze drains were inserted and the wound partially closed. The patient was very ill soon after the operation, requiring hypodermoclysis, but her condition quickly improved, and the next day she was in fairly good condition. Convalescence was uninterrupted, the wound healing rapidly. An



Due to the contraction of the gall-bladder, it was impossible to replace the stone in its original position at the mouth of the cystic duct.

interesting feature in the convalescence, however, was the leucocyte count. This stood at 37,600 on the morning of the operation; the next day it had dropped to 12,600; the count then rose again to about 15,000 to 18,000, and finally gradually subsided. The patient was discharged from the hospital on November 14th, with only a small superficial granulating surface remaining. This subsequently entirely healed.

The etiology of gangrenous cholecystitis rests probably on two factors, obstruction of the cystic duct and infection by virulent micro-organisms. Whether either of these alone would produce it could hardly be proved, since in all cases micro-organisms are present and

some form of obstruction, though it may result only from a swollen mucous membrane. It is hard to believe that gangrene of the organ could develop with a patulous cystic duct. Of course, gangrene of the gall-bladder does not occur until the inflammation has obstructed the circulation, and the fact that the gall-bladder is so well supplied with bloodvessels saves it from gangrene, no doubt, in many instances. The pathological lesions of the gall-bladder closely resemble those of the appendix, but gangrene of the one organ is rare and of the other common, and in all likelihood this is to be attributed to the poor blood supply of the one and the free blood supply of the other. In the case reported the cystic artery bled freely when the gall-bladder was removed, and yet the entire mucous membrane and all the coats of the fundus were gangrenous. In this case I believe gangrene resulted from the firm impaction of the large stone at the mouth of the cystic duct, cutting off, when inflammation became well established, the circulation in much the same manner as an appendolith does in the appendix. The way in which the omentum was found spread over and adherent to the fundus of the gall-bladder reminded one of the way in which it so frequently surrounds a gangrenous appendix.

Of the symptoms it will suffice to refer to those presented in the above case. In brief, they are those of a violent, localized peritonitis, with usually some temperature, persistent vomiting, obstruction of the bowels, and a high leucocyte count. Jaundice is not generally present unless there exists a marked cholangitis, or unless the inflammation has extended by contiguity into the liver structure.

The diagnosis of this condition may be confused with that of appendicitis. When an anæsthetic is administered, however, I believe that the two conditions can be differentiated and certainly immediate operation is equally called for in both. It would be a serious error to delay the opening of the abdomen in order to make a differential diagnosis between these two conditions.

The question of treatment probably ranks in interest next to the pathology. With the symptoms referred to no surgeon would hesitate to urge immediate operation, exactly as he would in the presence of similar symptoms referable to the right iliac region, and I believe that precisely the same treatment should apply to a gangrenous gall-bladder as applies to a gangrenous appendix. Some authorities have in phlegmonous inflammation of the gall-bladder recommended and practised simple drainage. This may be good surgery when the stage of gangrene has not been reached, or when the organ is small and contracted and its removal might result in death from shock, the result of a prolonged operation; but when the entire mucous membrane is gangrenous, and particularly when a portion of the whole thickness of the wall of the gall-bladder is gangrenous, total removal of the organ

is called for, and to leave it would be comparable to leaving a gangrenous appendix which had been freed from all its adhesions and lay well separated from the abdominal cavity by gauze pads. To drain and leave such a gall-bladder means continued absorption and probably an early death from sepsis. The relief following the removal of an organ in such a condition is well illustrated in my own case by the immediate cessation of symptoms and a fall in the leucocyte count from 37,600 to 12,600 in twenty-four hours. Regarding the technique of the procedure of cholecystectomy in the presence of inflammation of even a milder type than was here present, I am convinced that the advice of Mayo, who states that the cystic duct should not be ligated, is sound, and I am exceedingly glad that in my case the gall-bladder separated and came away before I committed what I now believe would have been an error. There must, in all such cases, be considerable cholangitis present, and nothing gives such relief in this condition, or so quickly arrests it as external drainage.

JAUNDICE, WITH REPORTS OF INTERESTING ILLUSTRATIVE CASES—A CONTRIBUTION TO THE TOXIC FORMS OF THIS CONDITION.*

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Most writers upon the subject of jaundice arrange all cases under two heads—obstructive and non-obstructive, or extrahepatic and intrahepatic jaundice. The data at hand, however, are insufficient to permit of a clear discrimination and an accurate classification in this manner. Furthermore, several possible causes may exist in a given case of jaundice, and it is often difficult to discover which of these is the preponderating or active factor in the condition. In certain cases of obstructive jaundice there is associated a pathological condition of the blood, or of the hepatic cells, one or both. Hence, the great variety and uncertainty of the causes prevent a satisfactory classification at present writing.

There are few diseases of the liver and of the bile passages that are invariably unattended by jaundice. In this group, however, may be placed amyloid liver and fatty liver. On the other hand, there are many hepatic diseases and conditions in the course of which jaundice may rarely occur. Among rare instances may be mentioned chole-

* Read before the Academy of Medicine, Buffalo, N. Y., May 13, 1902.

cystitis, needles, fruit-kernels, distomata, and round worms in the choledoch duct; echinococci, stagnation of bile in the intrahepatic biliary passages, in consequence of interference with the descent of the diaphragm (as in diaphragmatic pleurisy on the right side), so that the propulsion of the bile from the liver to the intestine does not occur (Schuppell); inspissated bile, lipoma, and polypus growing from the wall of the biliary canal, secondary syphilis, and, finally, kinks in the common duct in consequence of displacement of the liver. Frerichs[1] speaks of jaundice caused by an accumulation of pigment in the canaliculi lying between the hepatic cells, as, for example, in malignant malarial fevers; also of an etiological variety occasioned by hemorrhage that drains the vena porta, as in yellow fever. In the latter event there occurs disturbance in the hepatic circulation, with abnormal diffusion of bile and, at times, jaundice. That a paralytic and spastic jaundice occurs, as the older writers contend, is more than doubtful. The commoner causes for both intrahepatic and extrahepatic jaundice are too well known to require enumeration here. Besides, I purpose to consider principally so-called toxic jaundice, giving brief notes of a few illustrative cases. It is sometimes impracticable to distinguish clinically between instances of toxæmic origin and those due to obvious obstruction. Moreover, the fact that, as previously stated, the different forms, etiologically considered, may co-exist is to be recollected.

In the course of numerous affections that are accompanied by profound toxæmia jaundice may be observed. The toxic form also arises from the action of certain poisons, as ether, chloroform, and the like. The question, Is there a true toxæmic or diffusion icterus? is no longer, as formerly, a vexed one. A number of hypotheses, however, have been advanced to explain its occurrence, with doubtful justifications in most instances. Liebermeister contends that under conditions of pathological change the liver cells cannot retain their secretions.

The theory of Cornil[2] probably explains the mode of origin of many cases at least; it is that the epithelial lining of the smaller bile ducts becomes swollen, and an obstruction is thus produced.

Within the past few years I have met with cases, some of which are reported below, that apparently tend to support in the main the view advanced by Frerichs, and upheld by Murchison,[3] that in many instances of toxic jaundice an excessive amount of bile pigment is secreted, with subsequent reabsorption of the redundant quantity from the intestines. It will be seen later that while the primary and striking pathological feature may be found in the blood, and the amount of bile secreted may be in excess, there is probably in all such cases of jaundice temporary obstruction in the fine biliary canals as the result of increased viscosity of the bile or an intrahepatic cholangitis; hence, reabsorption, not from the intestines, but from the liver, occurs. That

we have no means of determining with accuracy the quantity of bile generated per diem, however, is generally conceded, so that this theory lacks demonstrative proof; it rests solely upon clinical testimony. On the subject of polycholia due to ether narcosis, which falls under this head, the literature is peculiarly silent; this is even more true as regards the report of any undoubted cases. In this connection the case of jaundice reported below, following the anæsthetic state, seems worthy of being recorded:

CASE I.—Mrs. A. M. S., aged twenty-six years, childless, an actress, was admitted to the gynecological wards of the Medico-Chirurgical Hospital February 27, 1902, under the care of Dr. W. Easterly Ashton.

The family history revealed the death of the father from smallpox; also that of the mother from some unknown cause, and of one aunt who died of chronic Bright's disease. The patient had had some of the diseases of childhood; malaria at fourteen, with occasional recurrences since then; peritonitis when sixteen years old, lasting four months; from the age of thirteen until the present she has had tonsillitis at intervals. Since the attack of peritonitis the menstruation has been both profuse and painful. In September, 1901, she suddenly developed acute gastric symptoms, as eructations, with severe pain in the epigastric and the right hypochondriac regions. No history of jaundice appeared that could be elicited now, and the duration of the illness was about one week.

On admission (February 27th) the patient presented the symptoms of bilateral ovarian disease, and on March 4th was operated upon by Dr. Ashton. Cœliotomy revealed a pyosalpinx on one side and a hydropyosalpinx on the other. The case progressed favorably until March 7th (except for persistent vomiting, with retching, in consequence of the etherization), when there appeared slight fever and distress after the feedings; slight pains referred to the epigastrium, right hypochondrium, and the region of the small intestines. Up to this time the bowels had been confined, but now, as the result of a mild saline laxative, diarrhœa set in and soon became a troublesome symptom, there being six to eight movements in the twenty-four hours. The dejecta were of a dark greenish-yellow color in appearance, not offensive, and apparently contained much bile.

On March 12th jaundice appeared, but was slight; the next day the skin and scleræ showed a distinct, moderately deep, saffron hue, not much gastric but more intestinal disturbance, and low irregular fever. (See temperature Chart 1.) The physical signs indicated slight enlargement of the liver; moderate tenderness to palpation over the liver, more marked over the gall-bladder area and intestines. The abdominal wound was reported to be in good condition. Bradycardia absent. The urine analysis showed the presence of bile-pigment, traces of albumin, and a few narrow granular casts. In color it was a dark greenish-yellow, and when shaken displayed a yellow froth.

March 14th. Some pain, which at times radiates to the right shoulder and down the right flank, and tenderness over the region of the gall-bladder, but this organ could not be felt. The jaundice continued, and the urinary examination gave the same result as noted above. The stools still numbered six to eight daily, and were deeply bile-

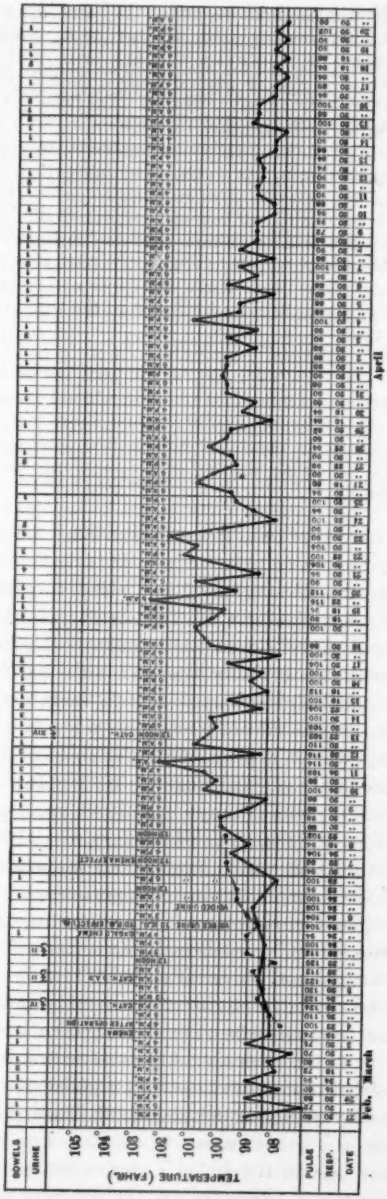

TEMPERATURE (FAHR.)
105°
104°
103°
102°
101°
100°
99°
98°
BOWELS
URINE
PULSE
RESP.
DATE
March
April

CHART 1.

stained. The blood examination gave the following result: Red corpuscles, 3,090,000; hæmoglobin, 60 per cent.; white corpuscles, 27,000. The increase in leucocytes affected principally the polymorphonuclear elements—a simple leucocytosis. A few poikilocytes and nucleated red cells were noted. March 17th, the jaundice and the local symptoms began to disappear.

19th. The skin and conjunctivæ are almost free from discoloration; neither bile, albumin, nor casts were present in the urine, but the bowel movements are still frequent, seven to eight per day; dark greenish-brown in color and, on testing, contained bile pigment.

20th. Jaundice practically absent, patient comfortable except from pain in lower abdominal region. The stools were less frequent—three to four daily, and they contained less bile. About this time, or possibly a couple of days earlier, an abscess in the wound was discovered and properly treated.

April 4th. The patient's general condition greatly improved, the bowels were moving once or twice daily, and the stools presented a normal appearance. An examination of the blood resulted as follows: Red cells, 3,730,000; whites, 20,000; hæmoglobin, 69 per cent. The case is well advanced in convalescence, as the temperature chart also corroborates. At no time during the course of the jaundice was bradycardia present.

The nature of the jaundice in this case is difficult to determine. Was it a case of polychromia or polycholia? In this condition the jaundice results from the dissolution of red blood corpuscles, whereby a large amount of hæmoglobin is set free in the blood current and is converted by the liver cells into bile pigment. The increased formation of bile pigment is invariably attended with increased viscosity of the bile, and the altered, inspissated, hepatic secretion opposes a temporary obstruction to the onward movement of the bile, followed by its absorption. This position is pretty firmly established from the experimental side by the labors of Stadelmann,[4] W. Hunter, Minkowsky and Naunyn.[5] Minkowsky and Naunyn submitted geese and ducks to the action of arseniuretted hydrogen, both before and after extirpation of the liver, and found that while hæmoglobin is present in the urine after removal of the liver, bilirubin is always absent.

Commenting upon the more recent experimental investigations into so-called "hematogenous" jaundice, Lazarus-Barlow[6] states: "It is now generally, though not universally, held (1) that a hematogenous jaundice does not exist; (2) that all varieties of jaundice are hepatogenous and due to reabsorption of bile formed in the liver; (3) the reabsorption is due to the presence of an obstruction in the bile ducts, whether this obstruction is obvious—*e. g.*, a gallstone—or not. Jaundice, therefore, only occurs as the result of blood destruction, when the liver seizes on the blood pigment, converts it into bile pigment, and returns it in bile to the blood." Since neither the polychromia nor the polycholia would occur without the primary blood destruction

in these cases, Murchison has suggested that the term "hematogenous" is appropriate in a certain sense, at least.

The evidence before adduced renders it certain that in all cases of jaundice an impediment to the onflow of the bile exists, or, in other words, that the liver is necessary to the production of jaundice. The term "hepatogenous" jaundice may be, therefore, appropriately applied to this symptom in every instance, but it seems to me that it would be advisable to regard as obsolete the term "hematogenous" and to retain that of "toxæmic jaundice" to designate such cases of hepatogenous form as that reported above, as well as all others in which blood destruction is a strong pathological feature. The increased hæmolysis in my case, if it actually existed, was most probably due in great part to the ether. The question, however, arises, Was not the jaundice dependent upon a cholecystitis associated with biliary obstruction? While some of the clinical symptoms and signs bore a close resemblance to cholecystitis, the nature of the dejecta and the brevity of the attack would tend to exclude the latter affection.

Moreover, the local phenomena were scarcely of sufficient intensity to warrant a diagnosis of suppurative cholecystitis; and the physical signs were too indefinite to be of diagnostic value. Again, owing to the slight suppuration in the wound, the presence of leucocytosis and irregular fever, the jaundice might be attributed to a septic process. It is to be recollected, however, that the slight septic symptoms persisted after the jaundice had disappeared. Moreover, in my experience, jaundice of the same degree of intensity has never occurred in so mild a grade of septicæmia. Was the patient affected with a duodenitis that acted as the causative factor? The usual section diet had been taken both prior and subsequent to the operation; it was not thought likely that this had produced duodenal catarrh. The presence of an apparently copious biliary secretion which was discharged per rectum also tends to exclude the possibility of the existence of obstruction in the common duct due to duodenitis. It was most probably true of my case that the abnormally large quantity of bile pigment suddenly generated occasioned an increased viscosity of the biliary secretion and consequent blocking of the hepatic canaliculi. This obstruction, however, was easily removed by a laxative, as compared with that due to catarrhal lesions, hence the comparatively short course of the jaundice. In my case bilious-looking stools promptly followed the administration of a saline laxative three days after operation.

As stated above, bradycardia was not present, while this symptom is the rule in instances of obstructive jaundice. The old view that bradycardia in pure hepatogenous jaundice is due to the action of the complete biliary secretion upon the heart, while in toxæmic jaundice the absence of the bile salts from the blood accounts for a normal

pulse rate in the latter variety, is no longer held. Strümpell contends that the infrequency of the pulse is due to the action upon the heart of the taurocholate of sodium. *Per contra*, as pointed out by Lazarus-Barlow, the assertion as to the absence of bile salts in toxic jaundice is not very reliable. Moreover, Stadelmann found them present in the non-obstructive jaundice caused by phosphorus, arseniuretted hydrogen, and other substances; and Naunyn found them in two cases of pyæmia in which the hepatic ducts were free. To account for the difference in respect to the pulse rate between toxic and hepatogenous jaundice is impossible at present writing. The extent of dissolution of the blood in the course of ether narcosis necessary to produce polycholia or polychromia is not known. The condition following the every-day run of operations is exceedingly rare, as shown by an examination of the literature. But that blood destruction occurs during the anæsthetic state has been absolutely proven. Da Costa and Kalteyer[1] have studied the blood in fifty cases, and have concluded that invariably etherization produces increased hæmolysis, following which the rapidly regenerated cells are imperfectly supplied with hæmoglobin. They believe that those who affirm the contrary are possibly misled by the blood concentration that results from the preliminary treatment which is often added to by the sweating during the anæsthetic state. These authors also maintain that the color index always falls and that the number of corpuscles always increases.

Through the kind aid of Dr. L. Napoleon Boston, I can give the results of a few experiments upon rabbits with ether administered by inhalation. The first series of experiments was upon two healthy female rabbits. The blood of each animal was examined directly before administering the ether, and again twenty minutes after the anæsthetic state was reached, at which time the ether was withdrawn. Forty minutes later (one hour after complete anæsthesia was reached) the blood was examined, and later daily until the animal's blood had returned to the normal.

EXPERIMENT I. Female rabbit, pregnant; weight 2 kilos, 130 grammes. Red cells, 4,462,500; white cells, 16,000; hæmoglobin, 60 per cent. Stained specimens presented nothing abnormal. Ether for twenty minutes (℥vj Squibb's). The red cells, 5,750,000; white cells, 24,000; hæmoglobin, 50 per cent. Red cells much distorted and presented decided variation in size, microcytes being numerous. A number of nucleated red cells (mostly normoblasts) were seen; many large polynuclear leucocytes showing irregular basophilic granules were observed.

One hour after ether: Weight 2 kilos, 110 grammes (lost 20 grammes). Red cells, 3,567,600; white cells, 24,000; hæmoglobin, 52 per cent. Poikilocytosis extreme. Microcytes and macrocytes numerous. Many crenated cells were seen in every field. White cells were at last noted.

Twenty-four hours after ether: Hæmoglobin, 30 per cent. Red cells are poor in staining properties, and often stain irregularly, some taking scarcely any of the eosin; poikilocytosis is marked. The polymorphonuclear leucocytes often contain large irregular granules, which are stained brownish by both the eosin and hæmotoxylin. Many cells resembling the "myelocyte" were also observed. Nucleated red cells (normoblasts) were not common.

Forty-eight hours after ether: Red cells, 4,500,000; white cells, 6000; hæmoglobin, 46 per cent. The red and white cells display but moderate variation from the normal. Seventy-two hours after ether, red cells, 4,980,000; white cells, 10,660; hæmoglobin, 47 per cent. One hundred and four hours after ether, hæmoglobin had reached 51 per cent., and on the following day 55 per cent. Otherwise normal.

EXPERIMENT II. Female rabbit, weight 3 pounds 3 ounces. Red cells, 3,960,700; white cells, 4200; hæmoglobin, 65 per cent. Twenty minutes after ether (℥iv Squibb's). Red cells, 4,375,000; white cells, 6500; hæmoglobin, 55 per cent. Poikilocytosis was marked, and crenated cells were not uncommon. Microcytes and macrocytes numerous. White cells appeared as normal.

One hour after ether: Weight 3 pounds. Red cells, 3,280,000; white cells, 8500; hæmoglobin, 58 per cent. Poikilocytosis extreme, and especially prominent is the variation in size of reds. Red cells do not stain equally. White cells, polynuclears, display many coarse, brownish granules. Nucleated red cells are not uncommon.

Twenty-four hours after ether: Red cells, 4,690,000; white cells, 6200; hæmoglobin, 43 per cent. Red cells stained irregularly, and many appeared as a mere shadow. Poikilocytosis was but moderate as compared to that observed in Rabbit No. 1. Crenated cells were common, as were also nucleated red cells. Forty-eight hours after ether: Hæmoglobin, 58 per cent. Otherwise as last noted. Sixty hours after ether: Red cells, 4,810,000; white cells 6800; hæmoglobin, 64 per cent. General appearance of stained specimens was as normal.

EXPERIMENT III. Female rabbit; weight, 1 kilo, 9845 grammes; was etherized for one hour, Squibb's ether (℥j) employed. Loss in weight 340 grammes. During the first twenty minutes hæmoglobin fell from 82 to 76 per cent., but at the end of an hour it had fallen to 72 per cent. During the following twenty-four hours the reduction in the hæmoglobin was very slight, and at the end of forty-eight hours it had returned to the normal. Leucocytes increased from 6200 to 13,000, while the red cells were, before ether, 6,230,000; twenty minutes after ether, 5,760,000; one hour after ether, 5,430,000; twenty-four hours after ether, 5,210,000; forty-eight hours after ether, 6,310,000; eight days after ether, 6,475,900. The changes in the stained specimens were practically those observed in connection with Experiment II., but were less pronounced.

With a view to determining as precisely as possible the effects of ether administered by inhalation upon the blood, a human subject was next selected, without any special preparation for an anæsthetic.

EXPERIMENT IV. J. H., male, aged thirty-three years. Irish extraction, who was apparently in perfect health, except for slight

ankylosis of the right knee, resulting from an injury, for which condition he was placed in my ward at the Medico-Chirurgical Hospital. His blood was examined May 1, 1902, which gave hæmoglobin, 86 per cent.; red cells, 4,280,000; white cells, 7600. Stained specimens were found to be normal in every respect. About five hours after a full meal (breakfast) he was given ether, Squibb's, for twenty minutes, at which time the ether was withdrawn and the blood examination repeated; hæmoglobin, 79 per cent.; red cells, 6,150,000; white cells, 16,000. There was no evidence of poikilocytosis; few microcytes were seen; all the erythrocytes stained normally. The increase in polymorphonuclear leucocytes was apparently well-marked. No myelocytes found.

An hour later, hæmoglobin, 74 per cent.; red cells, 4,170,000; white cells, 9800. Many of the red cells were seen to stain feebly with eosin, at times appearing as mere shadows, and there was decided variation in the size of the erythrocytes (microcytes). A differential count of the leucocytes gave polymorphonuclear, 81.91 per cent.; myelocytes, 4.94 per cent.; transitional, 10 per cent.; large mononuclears, 1.11 per cent.; small lymphocytes, 1 per cent.; eosinophiles, 1 per cent.

Twenty-four hours after ether it was reported that the patient had not vomited after the anæsthetic, and that he had taken food and drink twelve hours after the ether was withdrawn. His blood at this time gave hæmoglobin, 67 per cent.; red cells, 4,576,600; white cells, 13,600. Great variation in the size and staining properties of the erythrocytes was observed, and there was pronounced distortion of many of the larger cells. Certain cells stained unevenly, and the general appearance of these cells was not unlike those found in severe grades of anæmia. Leucocytes presented practically the same appearance noted at the previous examination.

Thirty hours after ether: Hæmoglobin, 78 per cent.; red cells, 4,620,000; white cells, 12,000. Forty-eight hours after ether: Hæmoglobin, 80 per cent.; red cells, 5,700,000; white cells, 10,600. At this time there was a decided increase in the number of small lymphocytes, yet the polymorphonuclear cells formed the greater portion of the leucocytes. Few myelocytes were present. The erythrocytes were apparently normal. Seventy-two hours after ether: Hæmoglobin, 86 per cent.; red cells, 4,780,000; white cells, 7400. On one side of the smears three myelocytes were found, otherwise a stained specimen appeared to be normal.

Experiment V. Animal used for Experiment II. was again etherized May 2, 1902 (seventeen days after the first anæsthesia). Animal now in apparently perfect health. Ether (Squibb's) was given for one hour and forty-five minutes. Blood examinations were made immediately before ether, and after the animal had been anæsthetized for one hour, and for one hour and forty-five minutes, respectively; also twenty-four hours and forty-eight hours after the anæsthetic had been withdrawn.

Before ether: Red cells, 3,016,600; white cells, 8000; hæmoglobin, 50 per cent. Stained specimens appeared as normal. One hour after ether: Red cells, 5,120,000; white cells, 12,000; hæmoglobin, 49 per cent. Slight poikilocytosis. One and three-fourths hours after ether: Red cells, 4,440,000; white cells, 13,600; hæmoglobin,

43 per cent. Total quantity of ether employed, 9 drachms. Red cells show great variation in both size, form, and staining properties of the erythrocytes. Cells staining but feebly are common, and usually these are distorted. Leucocytes appear to be normal as to varieties. Twenty-four hours after ether: Red cells, 3,820,000; white cells, 8000; hæmoglobin, 53 per cent. Crenated cells common, otherwise normal. Subsequent examinations revealed similar findings.

Second etherization of Animal III.

EXPERIMENT VI. Eleven days after first ether. Before ether was given, red cells, 4,730,000; white cells, 8000; hæmoglobin, 79 per cent. Stained specimens appear normal. Ether for twenty minutes, giving all the animal could take, hæmoglobin, 57 per cent.; red cells, 7,880,000; white cells, 8000; died five minutes later. Stained specimens showed great variation in the size of the red cells. All the red cells were extremely pale and poor in hæmoglobin except a few microcytes. Many crenated cells and poikilocytes were found. Microcytes were common and macrocytes numerous. Few nucleated reds (normoblasts) were also observed.

It is of interest in this connection to note, as shown by Experiment V., that during a second etherization, seventeen days after the first, the changes in the blood were less pronounced than at the first; also that this loss of hæmoglobin is restored in from twenty-four to forty-eight hours following the anæsthetic. Again, the duration of the anæsthetic state does not appear to influence materially the blood findings.

These few laboratory experiments show clearly that the fall in the color index in primary anæsthesia reaches its lowest level about twenty-four hours after the anæsthetic state is over; also that one-half of this fall takes place during the first hour after anæsthesia, the other half during the succeeding twenty-three hours. The blood regeneration goes on quite rapidly following the anæsthetic condition, but the hæmoglobin is restored more slowly than the erythrocytes; hence the cells are inadequately supplied with hæmoglobin. At the end of twenty-four hours the color index begins to rise rapidly, and it reaches the normal level after the lapse, approximately, of seventy-two hours in man. A few myelocytes, however, were still present at this time.

The polycythæmia noted does not depend solely upon the preparatory treatment, including purgation, since this was purposely omitted in some of the above cases (Case IV.). The decidedly increased blood production immediately following the administration of the anæsthesia would appear to be a factor in bringing about the polycythæmia according to our experiments. It seems to me that the suddenness with which a rather extensive blood destruction takes place during etherization accounts in a satisfactory manner for the occasional occurrence of polycholia, since there occurs an equally rapid liberation of hæmoglobin which, if acted upon by the hepatic cells, must result in an increased

amount of bile pigment. Of course, a mixed etiology may obtain in some cases.

CASE II. *Intense Jaundice in Connection with Lobar Pneumonia.*—C. E. V., aged fifty-three years; married; occupation, clerk; first came under my observation March 4, 1901. The family history showed the ancestors to have been unusually free from hereditary taint, except possibly slight traces of gout and hepatic torpidity in the father. The patient had no recollection of having had any disease of childhood, with the exception of measles. Social habits unexemplary; for many years he had suffered from alcoholic inebriety, and more recently had shown symptoms indicative of the early stage of hepatic cirrhosis. Analogous changes were believed to be present in the kidneys, as suggested by the urinary findings. Moreover, at the age of about forty years he contracted syphilis, and the changes in the liver were ascribed, in part at least, to the syphilitic infection. About three years prior to his death the patient had had pneumonia.

For several months previous to his last (fatal) illness the craving for alcohol seemed to be continuous and resistless; it was accompanied by an unusual degree of exposure to wet and low temperature. The last illness began as an influenza, lasting four days, when pneumonia affecting the lower lobe of the right lung set in without the usual ushering-in rigor and other severe invasion symptoms.

During the preliminary or influenza stage the temperature ranged from 99° F. to 101° F., and with the onset of the pneumonia it rose to 103° F., and finally to 104° F. The temperature curve was of irregularly continued type. The respirations varied in rate from 40 to 60 per minute, and the pulse continued to be regular, of fair volume and force until two days prior to death, when it grew quite rapid, compressible, and arrhythmic. Prune-juice expectoration was present. At the end of the seventh or eighth day of the illness signs of consolidation affecting the left base were also in evidence.

Jaundice of moderate intensity developed on the second day of the pneumonia and gradually deepened until it became intense; this was shortly before the fatal termination occurred. The stools were at no time infrequent, and always contained some bile pigment. During the last four days of life the dejecta numbered from four to six daily, and near the close were passed involuntarily. The urine contained bile pigment in abundance, a small percentage of albumin and tube casts, principally of the granular variety.

With reference to the bile pigment, it may be further stated that it appeared to continue to increase in amount as shown by the color of the urine, reaching its highest limit at the time of death, as was stated respecting the icteric discoloration of the bodily surface and conjunctivæ. Death was preceded by marked nervous disturbances—active delirium—signs of intense motor irritation, as shown by subsultus and coarse tremors. On account of the urinary findings, the nervous phenomena were ascribed in part to uræmia. Delirium tremens did not, as had been feared, carry off the patient.

Autopsy, twenty-four hours after death, by Dr. L. Napoleon Boston: Well-nourished male, apparently fifty years of age; everywhere the

skin was jaundiced to an extreme degree. There were also many small cutaneous hemorrhages over the chest and abdomen; the superficial veins of the abdomen were enlarged; there was a small umbilical hernia and slight œdema of the hands, feet, and ankles. The percussion note became dull over the right lung at the third interspace, extending downward to a point two inches below the costal margin. The left lung showed slight impairment of the percussion note at the base; only a small incision into the abdomen was allowed. Abdominal fat three inches in thickness; abdominal cavity contained some fluid (removed by undertaker). Viscera including the liver were jaundiced; the stomach showed slight congestion, probably post-mortem.

Duodenum showed no evidence of congestion at any point. The mouth of the ductus communis was in no way obstructed. Upon pressure over the gall-bladder bile escaped into the duodenum. The gall-bladder and ducts presented nothing abnormal on macroscopic examination. The edges of the liver were nodular, and at many points there were decided contractures—attempts at the formation of additional lobes. On the superior surface, near the junction of the right and left lobes, it was decidedly nodular (hobnail). Each of the small liver lobules stood out clearly and was surrounded by a rather broad band of yellowish tissue, which was depressed. The base of the right lung was consolidated, as was also a small portion of the left lung posteriorly. At several places the organ had been entered by the needle and injected with the embalming fluid. The kidneys were not examined for the reason that it was not permitted.

The report of the microscopic findings in the liver by Prof. Coplin was as follows:

The changes were those typical of fatty cirrhosis, with marked cholangitis affecting the intrahepatic excretory ducts. Extensive desquamation of biliary epithelium was observed, and the presence in the smaller bile ducts of bacteria resembling the colon bacilli.

Such cases as the above prove with complete certainty that in some instances of pneumonic jaundice, at least in which there is no obvious macroscopic obstruction to account for the symptom, the microscopic examination may reveal the changes of a cholangitis. J. E. Graham[8] affirms that the jaundice of cardiac insufficiency and of pneumonia is accounted for by the fact that the bile is secreted under low pressure, so that the changes in the circulation may cause it to flow from the cells into the veins rather than into the biliary radicals. Is it not a fact, however, that bile is ordinarily secreted under low pressure? According to certain observers it is of toxic origin, while still others believe it to be due to catarrhal lesions affecting the duodenum and larger excretory ducts of the liver. In the case reported above, the intrahepatic cholangitis was doubtless the active causative factor. May not the increased amount of bile pigment have set up an inflammation of the fine biliary ducts? The obstruction to the outflow could not have been complete, owing to the constant presence of biliary color-

ing matter in the dejecta. Hence, the toxic element may also have played no inconspicuous part in the causation of the jaundice. The *modus operandi* would be similar to that pointed out in connection with Case I. I have seen two additional cases in which the lesions of an ordinary catarrhal jaundice existed, hence the icteric tint may at times be solely dependent upon the latter changes.

Mallory[9] and Longridge[10] have called attention to foci of necrosis, which they claim are common to the acute infections, including lobar pneumonia. It is of two varieties, central or diffuse, and focal. In the former (central) the lesion begins in the centre of the lobules and spreads peripherally. Focal necrosis may rarely be due to the toxin of pneumonia. Neither form of necrosis, however, was found on histological examination of the liver from my case.

In 1898, Türck[11] showed that when the pneumonic infection is severe, or the patient has low vitality, nucleated red cells, principally normoblasts, and in a lesser degree also megaloblasts appear in the peripheral blood. Maragliano has observed "degenerative" changes in the red cells in severe cases. It is interesting to note that in the observations upon the effect of the anæsthetic (ether) on the blood of our rabbits, an increased number of nucleated red cells, mostly normoblasts, and other degenerative changes were observed. The point is that increased hæmolysis from any cause may induce similar blood changes, and may also be the cause, with the aid of the liver function, of a symptomatic jaundice, as before explained. Again, when the liver is the seat of chronic pathological change, as in the case just reported, the obstruction to the outflow of inspissated and abnormally viscid bile is far greater than in a previously normal organ.

In this connection I desire to direct attention to the question of the causes of death in this and similar cases. It is doubtless true of obstructive jaundice that death is, in the majority of cases, due to the underlying condition that induces the jaundice rather than to the icterus itself. In some cases, however, and more especially those in which an excess of bile pigment is generated, the poisonous effects of the latter may prove fatal. Bouchard regards the biliverdin as the toxic constituent. As clinicians we are not so much concerned with the question of the special ingredient of the biliary secretion that possesses the poisonous properties—a moot point—as with the fact that a serious and even fatal condition (so-called cholæmia) may be suddenly induced by this secretion.

Just how death is brought about from the poisonous action of the bile is imperfectly understood. Much depends upon the previous condition of the kidneys. Moreover, I am firmly of the opinion, based on personal observation, that an acute nephritis is often set up by the bile pigment in the process of elimination through a normal urinary

tract. This fact is corroborated by Case V. of my present series (*vide infra*).

It is rare, indeed, to meet with jaundice during the secondary stage of syphilis. Through the kindness of my friend and assistant, Dr. Boston, I am able, however, to present brief notes of an illustrative case:

CASE III.—M. C. D., aged nineteen years; American; prostitute; first came under observation June 10, 1897. Parents and four brothers living and fairly healthy; all, however, are alcoholics.

Past History. She had some of the affections of childhood, afterward continued in good health until six or eight weeks ago, when she developed an eruption, the remains of which show it to have belonged to secondary syphilis. The patient has no knowledge of an initial sore. Three weeks ago she noticed a swelling of the feet and abdomen, at the same time developing a yellow vaginal discharge. A pelvic examination showed a cervical discharge and a cervix that was ulcerated and bleeding. The conjunctivæ and skin were markedly jaundiced, and the feet swollen to twice their normal size. The heart sounds were weak, valvular, and distant, but fairly regular; the liver was enlarged and tender to pressure; otherwise the physical signs were negative.

June 22, 1897. There is a wave of fluctuation over the abdomen; temperature, 101°; pulse, 120; respiration, 24. The patient complained of pain in the region of the liver and at angle of scapula; abdomen much distended.

23*d*. The condition as noted yesterday, except temperature, now 102°, and respiration 30 and difficult; she sits pillowed up in bed; pain severe, and size of abdomen increasing. Lips and tongue fissured, the former bleeding; also oozing of blood from the nose and gums; slight systolic murmur at apex; vomited twice during the day; face distinctly puffy; intense jaundice.

Examination of Urine. Specimen porter color, specific gravity 1020; sediment heavy; reaction acid. Chemically it was found to contain considerable albumin and bile pigment, but no sugar. The microscope revealed bile-stained pus, tube casts (granular and epithelial), and epithelium (vaginal and vesical).

June 24*th*. On the following day the patient greatly improved both locally and generally, although vomits a dark coffee-colored material every few hours.

26*th*. Jaundice still marked; stomach non-retentive, all food and dark-colored fluid vomited; an examination of stools showed bile pigment, epithelium, etc., but no pus.

27*th*. Pain persists in abdomen, but there is no vomiting, and the jaundice is disappearing. At no time was there an absence of bile pigment from the stools. The patient now improved day by day under anti-syphilitic treatment, until at the end of four to five weeks all symptoms had vanished.

The cause of the jaundice in this instance was believed by Dr. E. P. Martin, who saw the patient by request, to be perihepatitis. According to White and Martin,[12] jaundice developing during the secondary period is rarely due to syphilis. The great majority of such cases,

when unattended by hepatic enlargement, as in the case herewith reported, are caused by intercurrent affections, such as a catarrhal condition of the bile ducts, "and are neither directly nor indirectly dependent upon constitutional syphilis." It is not likely that a gumma in the portal fissure was the cause of the jaundice in this case, as it had not progressed beyond the second stage. While the jaundice in this case was ascribed to the perihepatitis, although no blood examination was made, it is to be recollected that the syphilitic virus may cause extensive dissolution of the erythrocytes and marked oligochromæmia in the second stage of the affection. In this stage all forms of nucleated reds and poikilocytosis have also been commonly met with, especially when, as in this instance, the patients have belonged to the semi-starved, pauper element of society. The blood changes are identical with those characterizing toxæmic jaundice, and they may sustain an indirect causative relation to syphilitic icterus.

The question as to the cause of the fever in this case is an interesting one. Was it occasioned by acute nephritis? or by an intercurrent cholecystitis? or, finally, was it an instance of syphilitic fever? According to the results of the therapeutic tests, it was almost certainly ascribable to syphilis. Janeway[13] and others have reported cases in which fever attended the late manifestations of syphilis. It also occurs in the second stage. I have recently met with a case in a male, aged twenty-five years; it lasted about two weeks, and on several occasions the temperature rose to 102° F. Basset-Smith[14] reports a case in which a mis-diagnosis of malaria had been made on account of an intermittent fever curve. As the nephritic symptoms inducing dropsy disappeared under syphilitic treatment, they were doubtless of syphilitic origin. Allaria[15] also invites attention to early (secondary) syphilitic nephritis, with severe albuminuria, anasarca, and recovery under specific treatment.

Case IV. *Jaundice due to an intercurrent acute inflammatory condition in the course of hepatic cirrhosis.*—T. O. D., aged forty-four years; occupation plumber; single; admitted to the male medical wards of the Medico-Chirurgical Hospital, March 20, 1902. The family history is perfectly good, except that one sister died at the age of twenty-three years of some unknown cause. The patient had had none of the affections of childhood. Two attacks of acute articular rheumatism, the first at thirty years of age, lasting fourteen weeks, and the second at forty-one years, duration five weeks. During convalescence from the last attack of rheumatism, he drank heavily and steadily for a year or more, when he developed evidence of chronic nephritis, including dropsy of the feet and legs. He then abandoned alcohol, was placed upon appropriate treatment, and apparently recovered.

Shortly thereafter, or ten months ago, he had an attack of pneumonia, for which he was treated in the Medico-Chirurgical Hospital. Following this illness he again became intemperate, using whiskey in

excess; this he continued until date of admission. The illness that led him to apply for relief began six weeks previously, with indefinite symptoms, as fatigue, anorexia, constipation, and other prodromata of liver cirrhosis.

On March 19th (one day prior to admission) he developed intense pain in the region of the gall-bladder, radiating to the right shoulder, abdomen, and back. Fever developed; it was of irregularly continued type, and did not range high, the maximum temperature not exceeding 105.3° F. There were no rigors; the pulse was moderately accelerated (not slowed). The urine analysis at this time showed the presence of bile pigment, a small percentage of albumin and fine granular and epithelial casts. A physical examination indicated great enlargement of the liver, the lower border reaching to a line one inch below the umbilicus. The gall-bladder area was tender to the touch, but this viscus was not palpable. The second urine analysis, made March 25th, yielded results similar to those of the first, although the albumin was increased in amount to about 1 per cent. The skin was now a deep saffron hue. Fever more marked; patient quite delirious at night, exhibits noisy respiration, and is profoundly prostrated.

March 26th. All symptoms, including the jaundice rapidly abating; the liver is also diminishing in size. Albumoses searched for, but not found at any of the urinary examinations. The stools were not clay-colored, indicating no obstruction in the excretory ducts. This remission in the symptoms lasted a few days and then they reappeared, although less marked. (See Chart 2.)

31*st.* The jaundice returned with the recurrence of the fever.

April 17*th.* The temperature has been ranging near to the normal grade for one week, and the jaundice almost entirely vanished.

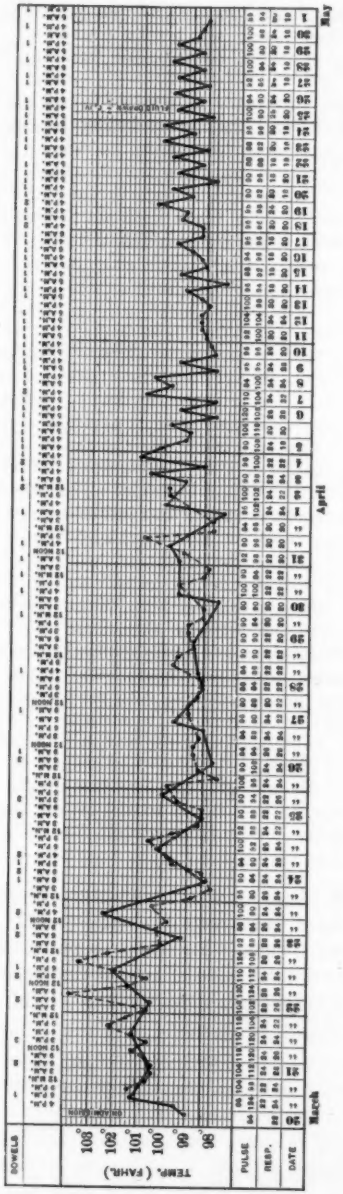
May 1*st.* The temperature has become nearly normal after a slight rise about ten days ago, and the patient has been growing stronger. Ascites has developed acutely during the past month; abdomen was tapped this day and 108 ounces of bile-stained fluid removed. A subsequent physical examination indicated only moderate hepatic enlargement, the organ having rapidly diminished in size during the previous two weeks. Very slight jaundice remained.

9*th.* Slowly improving. A blood examination resulted as follows: Reds, 3,790,000; whites, 9000; hæmoglobin, 55. Cells of normal size and form.

That cirrhosis may often be due to multiple causes is universally conceded. Again, many cases have as their principal etiological agent an infecting microbe. Thus tuberculosis, syphilis, malaria, one and all, may cause it. It is more particularly in the hypertrophic form of the disease that the etiology is often obscure. The case I have here reported is to be classed as alcoholic cirrhosis, according to the clear history. It is not unlikely, however, that as regards many cases of this variety of atrophic cirrhosis, our notions concerning etiology may be upset by future investigations.

Adami[16] affirms that in cattle the infective disease known as "Pictou disease" presents hepatic changes similar to those found in cirrhosis in man. The irritant in this case is believed to be a bacteriological toxin,

CHART 2.



which acts as a protoplasmic poison. Hektoen[17] reports a case of cirrhosis of the liver in animals, produced by a member of the colon group, and another that was caused by inoculation of the bacillus which belongs to the pseudodiphtheria group. Cultures were made from the bile-stained peritoneal fluid withdrawn in my case, with the following result: Bouillon cultures at twenty-four hours showed an abundant growth of motile bacilli, which on staining and further study were found to be members of the colon group. No other organisms were present in cultures. Slides were smeared with the peritoneal fluid, and when stained were found to show few bacilli which decolorized by Gram's method. No tubercle bacilli were found. The fluid was lemon-yellow in color, turbid, and presented a flocculent sediment; its specific gravity was 1010, reaction slightly alkaline, and contained about 0.12 per cent. of albumin.

This case also represents a group or class of cases that are by no means uncommon, and in which chronic hepatic disease, most commonly cirrhosis, is suddenly complicated with an acute inflammatory condition. In Case IV., just related, the intercurrent affection was regarded as being cholecystitis.

The principal features in this instance were similar to those of Weil's disease, namely, jaundice, fever, and albuminuria with casts. Rigors were absent, however, and the temperature curve closely resembled that of relapsing fever, as may be seen from a glance at the accompanying fever chart. (See Chart 2.) The intensity of the jaundice also corresponded pretty closely with the degree of elevation of temperature. This so-called relapsing jaundice must, it seems to me, be due to an infection and re-infection, but whether or not the colon bacillus is to be incriminated is still uncertain. Karlinski and others have described an epidemic jaundice of unknown etiology, in which the febrile movement pursued a similar course. These facts tend to prove the infectious nature of the condition, but it may be of varied etiology. H. Neuman[18] goes so far as to state that there is no demonstrable difference between epidemic infectious jaundice and simple catarrhal jaundice, which, he holds, is also due to an infection.

Case V. *Mixed cirrhosis, biliary and atrophic variety.*—This patient was under the charge of Dr. I. Newton Snively, to whom I am indebted for the notes of the case.

Mr. H. F., aged twenty-eight years; American; weight about 240 pounds; height 5 feet 10 inches; book-keeper by occupation. The family history is good, except that the father had been afflicted many years with epilepsy, and died from apoplexy.

Previous History. He had the ordinary diseases of childhood; measles, mumps, chicken-pox, and whooping-cough. As a boy he complained unusually of shortness of breath upon exertion, such as running and jumping, etc. He has been drinking quite heavily since he was nine-

teen years of age, and for two years and a half past has taken whiskey in enormous quantities, perhaps from a quart to a quart and a half every twenty-four hours; yet was never intoxicated so as to be unable to attend to his duties as book-keeper, etc.

About July, 1900, he noticed a sore on the right upper thigh about two inches back of the scrotum ; he attributed it to chafing, but as it refused to heal, he consulted Dr. Clifford Scott, who suspected specific infection, treated him accordingly, and in three or four weeks the sore healed. The patient was an inveterate smoker of cigarettes. Since twenty-one years of age he has been growing stouter, and for two years past has been extremely corpulent—in fact, almost helpless at times. One year before the onset of his present sickness he noticed a dropsical condition of the lower limbs, which later involved the scrotum, and he suffered greatly with shortness of breath, especially upon exertion. He was obliged to sleep propped up with head-rest and pillows for several months. His appetite, however, was enormous, and he ate largely of all kinds of food until the beginning of the present sickness.

The above symptoms, œdema of the lower limbs and scrotum, shortness of breath on exertion, etc., grew gradually worse until on November 29, 1901, he was compelled to stay in his room. At this time the abdomen was enormously enlarged, the limbs and scrotum were swollen to their utmost capacity and were oozing fluid. His pulse and respirations were rapid, as shown by the chart. He was tapped in the abdomen and scrotum a number of times; also the limbs.

Physical exploration, after paracentesis, by palpation and percussion showed an enormously enlarged liver. I saw the patient several times in consultation with Dr. Snively at intervals of several days. During the last month of life the temperature ranged from 99° to 102.3° F., ending with hyperpyrexia (see Chart 3); this was accompanied by delirium, prostration, and other evidences of an acute infection, without our being able to recognize the nature of the morbid process. The skin and conjunctivæ had been jaundiced for about three weeks before death. The tappings show that up to December 7, 1901, 384 ounces of fluid had been drawn off; also estimated 64 ounces on December 8th, which simply represented the oozing from scrotal openings made by the trocar and the oozings from the legs where the trocar had been used. The charts show several later tappings. Urinary analysis showed no sugar, albumin, or casts, except during the last four or five days of his life, when the urinary findings characterizing acute nephritis developed. He died January 4, 1902.

Post-mortem findings twenty-four hours after death by Dr. L. Napoleon Boston: Body of a male, large in stature, face swollen, and skin and conjunctivæ jaundiced. The veins over the abdomen and chest were dilated. A dull percussion note on the right side, commencing three inches above nipple and extending to crest of ilium. On opening the chest 100 c.c. of bloody fluid was found in each pleural sac; right lung pushed up to third rib and the arch of the diaphragm lifted to the same point in nipple line. Hypostatic congestion rather extensive in the left lung, and confined to the base of right lung. The myocardium was contracted, its walls thin, and showed fatty changes on section; the chambers were occupied by dense fibrous clots. Microscopic study of the heart muscle impossible, owing to the embalming fluid. The stomach was normal except that its walls were slightly congested,

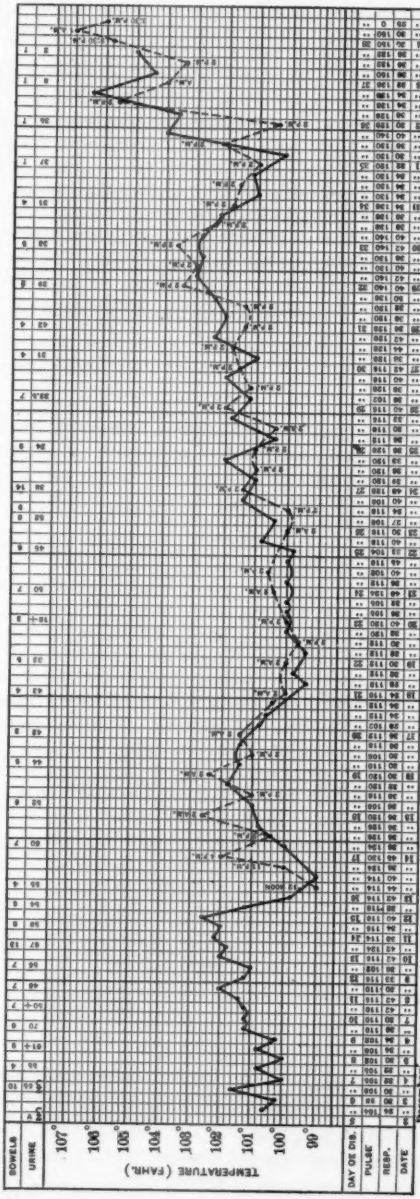

TEMPERATURE (FAHR.)
107°
106°
105°
104°
103°
102°
101°
100°
99°
98°
BOWELS
URINE
DAY OF DIS.
PULSE
RESP.
DATE
January
December

CHART 3.

but the ductus communis choledochus was patulous, and a needle could be passed directly into the gall-blader. The gall-bladder was normal and contained about one-half ounce of bile.

Liver. Weight 6040 grammes; color a greenish-yellow, surface smooth, slightly mottled, capsule free, and edges rounded. On section, resistance to the knife was increased; the surface presented a rather granular aspect; the acini were uniformly prominent, elevated, and each surrounded by a band of yellowish-white tissue, which showed slight depression. The needle of the embalming trocar had pierced the organ at several points, hence attempts at section for microscopic study were not altogether satisfactory, although the appearances were in the main those of fatty cirrhosis of the organ. The liver tissue was everywhere clearly and distinctly bile-stained. The kidneys presented the usual naked-eye appearance of acute nephritis, and this was also shown by microscopic study.

A microscopic examination of the liver by Dr. Coplin revealed the following:

"There is a large amount of elastica, which is intralobular and interlobular; enters lobules and often surrounds columns of cells, and at points is increased around smaller bile ducts, and is still more increased around the larger biliary branches. Newly-formed tissue between lobules, which is, for the most part, young and fully formed; fibrous tissue is not so abundant as the gross specimen would have led one to believe. The liver cells show fragmentation of protoplasm and nuclei, and advanced granular degeneration is evident in many cells. Young cell deposits are present, even within the lobules. Uniform fatty infiltration is fairly evenly distributed throughout sections.

"Epithelium of bile ducts is advancedly granular, often fragmented, and often desquamating. Evidence (distinct) of new bile duct formation is wanting. Many of the lobules show intense bile-staining, more pronounced at periphery than at centres. The lobules showing less fatty infiltration, least fragmentation of cells, and least young cell invasion and increase of elastica, are most stained with bile (and are probably secreting bile). Many stained cells are shrunken. Mixed cirrhosis, biliary, and fatty alcoholic varieties."

The features of greatest clinical interest in this case are the intense jaundice, the fever, and the acute nephritis coming on in the course of cirrhosis. A glance at the temperature chart will show that hyperpyrexia, with tendency to daily increase of fever, supervened two days before the occurrence of the fatal termination. The curve also shows a disposition, though incomplete, to relapsing febrile jaundice. Bradycardia was not present at any time; on the other hand, the pulse was accelerated throughout, and during the last three weeks of life much increased in frequency. The post-mortem failed to reveal any localized inflammatory or other lesions, save those of the liver and kidneys, to account for the fever, and it should be recalled that the urinary findings were negative up to within a week of the fatal termination. It seems to have been an instance of febrile jaundice arising in the course

of hepatic cirrhosis with the secondary development of acute nephritis. The case bears out the view previously expressed, namely, that febrile, infectious jaundice may be complicated with nephritis, and the latter condition may result from irritation of the renal tissue by the bile pigment in the process of elimination from the system. It is to be borne in mind, however, that in many of the acute infections nephritis due to the local irritant effect of the special toxin is not very uncommon. Uræmic symptoms attended near the close in Case V.

In conclusion, while the cases reported above do not furnish a basis for definite, conclusive inferences, they suggest a few queries and propositions:

1. Is there a true polycholia due to the conversion into bile pigment of the hæmoglobin that is suddenly liberated by certain poisons, as ether, chloroform, and the like, or the toxins of the acute infections, as, for example, lobar pneumonia?

2. Doubtless other causative agents are often operative in cases that fall under 1.

3. As there could be no jaundice without the presence of the liver, the term "hematogenous" is misleading, and should be regarded as obsolete; the term "toxæmic jaundice" may be, however, appropriately applied to the cases of "hepatogenous" icterus, in which the blood changes are a more or less striking pathological feature.

4. May not the jaundice rarely seen in secondary syphilis be toxic in nature, at times at least, rather than purely "hepatogenous?"

5. Admitting that there are well-established causes for the hepatic cirrhosis, more particularly of the atrophic form, the etiology is but imperfectly understood.

6. Clear evidence to show that the hepatic cirrhoses are, in many cases at least, of microbic origin is accumulating.

7. The intercurrent acute inflammatory conditions with jaundice in the course of cirrhosis of the liver are doubtless micro-organismal in nature. (See Cases II., IV., V.)

8. Relapsing febrile jaundice is also to be classified as an infection; it will probably be shown on further investigation to be due to a member of the colon group. (See Case IV.)

9. It is probable that the jaundice of hepatic cirrhosis is, in a certain sense at least, toxic in nature.

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ABSCESSES OF THE LIVER FOLLOWING TYPHOID FEVER.

By John G. Sheldon, M.D.,
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John H., aged thirty-four years, came to me June 24, 1901, complaining of pain in the right side; chilly feelings and sweats, and great weakness. He said that three days before he saw me he had left his bed, where he had been confined for six weeks suffering from a disease diagnosed by his attending physician as typhoid fever. The history of this illness was typical for an ordinary case of typhoid fever, except that he felt that he was regaining strength very slowly, and that he had felt a heaviness and dull pain in the right side during the last week that he remained in bed.

The patient's previous history was negative. He suffered from measles when a child, and had smallpox when twenty years of age, but had had no other illness.

The examination showed a well-developed, poorly-nourished and emaciated middle-aged man. His skin seemed somewhat darker than normal, but he was not jaundiced. The mucous membrane of the lips and conjunctivæ was pale. There was marked tenderness in the region of the liver, and I inferred from the physical findings that the liver was diffusely enlarged. Its lower border was well defined and extended a hand's breadth below the costal arch at the outer border of the right rectus muscle. The upper border of relative hepatic dulness extended, in the right mammillary line, to the upper border of the third rib. Examination of the chest showed diminished expansion and respiratory excursion on the right side. The apex of the left lung seemed duller than normal. Harsh breathing was found in the apex of the left lung and over the lower portion of the right. A few moist râles were present in both lungs posteriorly. No friction rubs were heard. The heart was slightly enlarged transversely, and a systolic murmur was present over the pulmonic area. No thrills were found. The pulse was beating 108 times per minute; was not strong, but was regular. The temperature was 101° F. The spleen was not felt. There was no tenderness in the lower abdominal region; and no evidences of fluid in the peritoneal cavity could be found. The remainder of the examination was negative. The urine showed a trace of albumin, but was otherwise normal.

A diagnosis was not made at this time. A diagnosis of cardiac insufficiency, with passive congestion of the liver, was not warranted.

Tuberculosis and syphilis could not be positively excluded, but the symptoms led us to suspect the presence of an inflammatory condition in the liver.

The developments in the case were as follows:

June 25th. Chill in the evening, followed by sweating. Temperature, 102° F.; pulse, 120. Pain in right side severe. Blood examined for malarial organisms—none found.

26th. Morning temperature 99° F. Slight chill at 2 P.M. Temperature, 8 P.M., 100° F.; pain continuous; tenderness marked.

27th. Leucocyte count, 18,000; differential count not made. No tubercle bacilli found in the sputum.

The patient remained about the same during June 28th, 29th, and 30th. His symptoms were gradually increasing in severity, and his liver was becoming larger. Several punctures were made into the right hepatic lobe from behind, and on the evening of June 30th I introduced a needle between the eighth and ninth ribs about three inches from the spine, and at a depth of five inches, withdrew about a drachm of thick, yellow pus.

Owing to the marked enlargement of the liver anteriorly and to the absence of signs of pleural adhesions, I decided to attack the liver from in front, and on July 1st an incision, three inches long, was made parallel to the right costal margin, the centre of the incision corresponding to the outer border of the right rectus muscle. The liver was smooth, and many small yellow areas were seen on its surface. No adhesions between the peritoneum and liver were observed. The peritoneal cavity was protected with gauze, after which an aspirating needle was introduced into the liver and pus found at the depth of about one inch. This abscess was opened with a blunt artery forceps and contained about a drachm of pus. Another abscess was located to the right of the first and was drained through the same opening. The bleeding became free, but was easily controlled by a pack or by introducing the finger into the liver wound. By using the needle, uterine probe, artery forceps, and finger, I located and drained five abscesses, none of which contained more than two drachms of pus. I then introduced a rubber tube, wrapped the gauze into the wound, and packed the lumen of the tube to prevent hemorrhage. The anæsthetic which consisted of $\frac{1}{100}$ of a grain of hyoscine hydrobromate, and $\frac{1}{4}$ of a grain of morphine hypodermically, followed in one-half hour by ether, was taken nicely, and the operation, which was of short duration, was not attended with much shock.

The patient slept five or six hours after the operation, after which I removed the pack from the lumen of the tube. A considerable amount of pus and bile, with some blood, escaped. Eight hours after the operation the patient's temperature was 100° F., his pulse 106. He had very little pain—less than before the operation—and said that he felt relieved. For one week the drainage was profuse, and the liver diminished markedly in size. The temperature rarely came down to normal, but the pulse remained good, and very little pain was complained of. The tube was removed on the sixth day following the operation and a gauze drain substituted. On July 10th the patient had a chill; his pulse was 118; temperature, 102° F., and he complained of considerable pain in the right side. Examination showed no changes in the physical findings—the liver dulness extended, pos-

teriorly, as high as the eighth rib. A uterine probe was introduced deeply into the liver wound and a small amount of pus was discharged. This did not give the patient relief. The chills and fever recurred and the pain continued, being situated more posteriorly than usual.

On July 16th the liver flatness extended to the lower border of the scapula. The anterior margin of the liver was found to be about one finger's breadth below the costal arch. There was no respiratory excursion on the right side. Under local anæsthesia a section of the ninth rib was removed in the posterior axillary line. The pleura was opened and not found adherent to the diaphragm. Twelve hours later pus was located at a depth of two inches from the base of the wound, and a large abscess cavity was opened by using a blunt artery forceps. A drainage tube was inserted. The patient felt relieved, the chills ceased, and the temperature and pulse became better. The patient at this time was very weak and somewhat emaciated. He got along very comfortably until August 1st, when he developed a cough. Pus still continued to discharge through the operation wound—the tube having been removed. From August 1st to August 10th the patient gradually failed. The pulse was weak and beat from 110 to 130 times per minute. The temperature was irregular, ranging from 100° to 101° F. No decided chills were complained of. The cough became more severe, and on August 8th blood was expectorated. On August 9th the patient complained of difficulty in breathing. On August 10th the dulness had extended higher on the right side than it had been previously. No movable dulness was made out. I introduced an artery forceps into the wound and opened the pleural cavity in an upward direction. The opening was dilated and a tube inserted. The improvement following this procedure was slight. On August 15th I explored the pleural cavity with the finger, broke up some adhesions and liberated a considerable amount of pus. The patient failed gradually. On August 20th he developed a diarrhœa, which lasted until August 22d, when he died.

The autopsy was done August 23d. The external examination of the body was negative, except for the presence of the two operation wounds. No icterus present.

The peritoneal cavity contained a small amount of clear, straw-colored fluid. The peritoneal surfaces were everywhere smooth, except that there were a few adhesions over the right lobe of the liver.

The pericardium contained a small quantity of clear fluid. Its surfaces were everywhere smooth. The heart was small, weighed 225 grammes. The myocardium was pale and friable. The cardiac valves were normal.

Many adhesions and a small quantity of pus were found in the right pleural cavity. The apices of both lungs were adherent. The lower portion of the left pleural cavity was normal. The pleura on the right side was markedly thickened.

The lower lobes of both lungs were hyperæmic, especially in the posterior parts. In the apex of the right lung several irregular cicatrices were found. A small cavity and a few scars were found in the apex of the left lung. The middle lobe of the right lung was firm and cut with resistance. Muco-pus could be squeezed from the bronchi. The bronchial glands were slightly pigmented. Calcareous deposits were found in two of them. There was found an opening in the diaphragm

—large enough to admit the index finger—which communicated with a cavity in the right hepatic lobe.

The liver weighed 1650 grammes. The right lobe presented a cicatrix and an irregular depression over its anterior surface. The posterior part of the right lobe was adherent to the diaphragm. On section the right lobe showed many irregular cicatrices in its anterior part. Situated in the posterior part of the right lobe of the liver was a globular cavity, 7 centimetres in diameter, communicating with the right pleural cavity through an opening in the diaphragm. This cavity contained dark-colored pus. It had no definite lining membrane. The liver tissue surrounding the abscess cavity was hyperæmic and friable.

The left hepatic lobe was enlarged in proportion to the size of the right. On its inferior surface five globular abscess cavities could be seen. These abscesses measured from 2 to 4 centimetres in diameter, and projected from the surface of the liver. On section the left lobe contained many abscesses, most of which were small. All of them had a definite lining membrane; and all of the smaller ones could be found to communicate directly with a branch of the portal vein. Pus could be squeezed from most of the portal vein radicals.

The biliary apparatus seemed normal; as did the hepatic artery. The splenic, portal, and superior mesenteric veins showed no gross abnormal lesions.

The lining of the small intestine was hyperæmic. No ulceration was found. Two Peyer's patches near the ileocæcal valve were elevated and indurated. The remainder of the patches presented a shaven-beard appearance. The serosa of the small intestines was normal. The mucosa of the large bowel was hyperæmic. Otherwise, the large intestines were normal.

The appendix showed no abnormal changes. The mesenteric glands were enlarged and indurated. Softening was found in the interior of one gland, 2 centimetres in diameter.

The kidneys were slightly larger than normal. Their capsules were not adherent. On section they were granular and friable, but otherwise they presented nothing abnormal. The remainder of the examination revealed nothing of interest. The nervous system was not examined.

The succession of pathological changes leading to the patient's death were believed to be as follows:

Typhoid fever; carrying of infectious material from the intestines or mesenteric glands by the portal vein to the liver; suppurative pylephlebitis, with abscess formation. The injury to the liver tissue done at the first operation resulted in the formation of a large abscess, differing from the smaller abscesses by being surrounded by a zone of hyperæmic liver tissue, and by being destitute of a definite lining membrane. This abscess might be classed as a secondary pyosepticæmic abscess, as described by Andrew Davidson.[1] The empyema resulted from the second operation.

The diagnosis of typhoid fever was made from the clinical history and from the post-mortem findings in the intestines. A Widal reaction

was not tried. Slides made from the first operation and from the small abscesses found in the left hepatic lobe on post-mortem examination showed the presence of a small bacillus, which might have been either the typhoid or the colon bacillus. However, typhoid fever seems the most probable cause for the patient's primary sickness.

The belief that the hepatic abscesses resulted from diseased portal vein radicals was supported by the finding of a suppurative pylephlebitis post-mortem and by the abscesses—especially the smaller ones—communicating directly with a branch of the portal vein. Infection of the liver by way of the arterial current was improbable. Although Hewlett[2] states that typhoid bacilli are found in the blood in 83 per cent. of the cases of typhoid fever, and Courmont[26] believes that typhoid septicæmia is the rule, the absence of changes in the arteries and the absence of suppurating foci in other parts of the body speak strongly against arterial infection in this case.

Suppuration in the liver following typhoid fever is a rare condition. Holscher reports that 12 cases of liver abscesses occurred in the 2000 fatal cases of typhoid fever at Munich. Romberg reports 1 case of liver abscess from 88 fatal cases of typhoid. Scholtz reports 3686 cases of typhoid fever, 362 of these cases died, and in none of them was suppuration in the liver found. Da Costa[3] has collected 22 cases of liver abscess following typhoid fever. Osler[4] makes the following statement concerning the occurrence of abscesses of the liver following typhoid fever: "Solitary abscess is exceedingly rare and occurred in but 2 cases in my series." Julius Dreschfeld[5] says: "Acute yellow atrophy of the liver and abscess of the liver may be cited as very rare complications." I believe that it is impossible to say, with any degree of accuracy, in what proportion of fatal cases of typhoid fever liver abscess is found. During my experience as a medical student, as an interne in Cook County Hospital, and in private practice, I have knowledge of the post-mortem findings of about 200 cases of typhoid fever. The case herewith reported is the only one in which I believe that suppuration in the liver was found.

The relation of the typhoid bacillus to hepatic suppuration has not been determined. It is possible that the suppuration is due to the presence of the typhoid bacillus alone. I am unable to find the record of a case in which the typhoid bacillus alone was found in a liver abscess that followed typhoid fever. Lannois[6] reports a case from which he isolated the typhoid bacillus, but the colon bacillus was also present. It is true that typhoid bacilli are found in pure cultures in the liver in cases of typhoid fever,[7] but in these cases no inflammatory reaction is present. As yet we have no proof that typhoid bacilli alone are capable of producing an abscess of the liver in patients suffering from typhoid fever. Bindo de Vecchi[8] has shown that the liver is insuscep-

tible to infection with certain organisms. The hepatic resistance may explain the inability of the typhoid bacillus to produce liver abscesses in cases of typhoid fever.

The colon bacillus is, in all probability, the organism that is most active in producing the so-called typhoid liver abscesses. In support of this theory are the following facts:

1. Colon bacilli are present in the abscesses of the liver following typhoid fever.

2. Roger[9] has shown that the liver promotes the growth of the colon bacillus, while it inhibits the growth of the typhoid bacillus.

3. Macaigne and Kleck[10] have shown that the virulence of the colon bacillus is increased by disorders of the intestinal tract.

4. Sanarelli[11] found that colon bacilli, isolated from typhoid stools, were more virulent than when isolated from healthy stools. He thought that the increase in virulence is due to the effect of the typhoid toxins, and devised an ingenious experiment which seems to prove this point. If it is true that the virulence of the colon bacillus is increased in a patient suffering from typhoid fever, and that the liver offers little if any resistance to invasion by the colon bacillus, it is not surprising that hepatic suppuration occasionally follows typhoid fever.

The organisms that are responsible for the production of hepatic abscesses following typhoid fever, reach the liver by way of the portal vein, the hepatic artery, or the bile-ducts. Infection through the portal vein seems to be the most common. In these cases it is probable that the organisms reach the portal vein from the intestinal walls or from the mesenteric glands. They are lodged in the portal radicals in the liver and there begin the process of abscess formation. In these cases the liver is usually diffusely enlarged and many abscesses are found. The abscesses have a well-defined wall—or lining membrane—and the smaller ones can be seen to directly communicate with the branches of the portal vein. The liver tissue surrounding the abscess, especially the smaller ones, does not show marked inflammatory reaction. Usually the findings in the liver are independent of changes in other parts of the body, and suppuration in other organs is uncommon in hepatic abscesses following pylephlebitis. The cases reported by Lannois, Osler, Romberg, Gerhard, Trougel, Buckling, Asch, and Bernhard and the case herewith reported are examples of portal vein infection.

Abscesses of the liver—following typhoid—due to infection by way of the hepatic artery are more rare than the variety described in the foregoing. Cases, however, are reported by Louis, Chvostek, Sidlo, and Barth. In these cases the liver may or may not be enlarged. If enlargement does occur it is rarely uniform. The abscesses are usually single or few in number. They are apt to be of large size, with no

well-defined lining membrane and not connected with the portal vein radicals. Abscesses in other regions of the body is the rule and not the exception. There was an abscess in the parotid in Louis' case. Suppurative perichondritis of the larynx was found in Chvostek's case; and in Sidlos' case an abscess was found in the mastoid region. In these cases it is probable that the colon bacillus as well as the typhoid bacillus is floating in the blood stream. I make this statement because such cases are rare and typhoid septicæmia, as Hewlett and Courmont (loc. cit.) have shown, is common.

The third method of infection of the liver, with abscess formation, namely, by way of the bile tracts, is not common. Klebs alone reports a case of this character. Suppurative cholangitis occasionally follows typhoid fever, but I am unable to find reports of cases of well-defined liver abscesses following typhoid fever in which the organisms have been carried to the liver by the bile channels. The pus in these forms of abscess, described in the foregoing, is usually of a white or yellowish-white color. I can find records of hemorrhagic or dark-colored pus occurring only in cases where secondary pyosepticæmic abscesses were present—that is, where abscesses were ruptured either by operation or by invading some cavity of the body. In these cases the abscess cavity has no "pyogenic membrane," the pus usually contains blood and is dark colored, and the liver tissue surrounding it shows marked inflammatory reaction. The abscess found in the posterior part of the right hepatic lobe in the case herewith reported was one of this character.

The symptoms of hepatic abscess following typhoid fever are: 1. The general symptoms of an infection. 2. Local manifestations pointing to involvement of the liver. Occasionally there are no symptoms complained of that would indicate hepatic involvement. Such cases are recorded by Theodore Dunin[13] and by Osler.[13]

The cases of liver abscess following typhoid that I can find records of occurred in adult males from twenty-five to thirty-seven years of age. One case occurred in a boy, aged twelve years, and another in a girl, aged eleven years. In none of the cases was there a history of previous disease involving the liver.

The first indication of involvement of the liver was manifested by pain in the hepatic region, accompanied by chills and fever. These symptoms occurred in all of the cases that I have reported, except the two mentioned in the foregoing, in which no symptoms referable to the liver were present. The pain and chills usually came on about twenty-five days after the onset of the illness. In one case[14] they occurred as early as the thirteenth day; and in two cases—Lannois[15] and the case herewith reported—they did not appear until the forty-second day.

Pain was present in all of the cases but two. It was usually of a

severe, sharp character, but in some cases was described as being dull. It was usually located in the region of the liver; was generally increased by inspiration, and in one case[16] was aggravated by taking food. In no case was the pain intermittent or paroxysmal; and in no case did it cease until the pus was relieved from tension, either by spontaneous rupture,[17 18] or by operation. Violent, prolonged, and repeated chills were present in most cases. Dunin[12] mentions the absence of chills in his case. In no case did the chills present the regularity that might be expected in malaria.

Jaundice was by no means a constant symptom. Da Costa[3] reports jaundice in 7 of the 22 cases that he has found recorded. It was present in the cases reported by Romberg,[19] Kohts[8] (Case I.), Sidlo,[17] Petrina,[14] Louis,[20] Chvostek,[21] and Burder.[22] In these cases jaundice occurred as early as the thirteenth day,[14] and as late as the thirty-ninth day[17] after the beginning of the illness. Jaundice occurred in cases with abscesses in other portions of the body,[17 18] and in cases where suppuration was found only in the liver. It does not appear that jaundice is present more often in cases of pylephlebitis than in cases of infection by way of the hepatic artery.

In most cases the liver was enlarged. Usually the enlargement was diffuse, but in some cases the right lobe was affected alone. In Bauder's, Lannois', and Dunin's cases no enlargement of the liver was found clinically or at post-mortem examination. In Gerhard's case,[23] fluctuation was present over the right hepatic lobe. In all cases where the liver was enlarged, marked tenderness was present.

Ascites was present in one case of pylephlebitis,[6] but no record of ascites is found in a similar case reported by Asch and Bernhard.[24]

No constant or characteristic condition was found in the spleen. Mention was made of its being enlarged in 3 cases. Thrombosis was found in the splenic veins in Lannois' case. I have not found record of splenic suppuration occurring in any case.

Suppuration in portions of the body other than the liver occurred in 7 of the cases. These may be divided into two classes: 1. Suppuration in the mesenteric glands. 2. Suppuration in other portions of the body. In the cases described by Romberg, Kohts, Louis, and the one herewith reported, suppuration was found in the mesenteric glands. Cases coming under Class II. may be divided into two groups: 1. Cases complicated by empyema. 2. Those associated with pus foci in distant regions of the body. I make this division because it is possible that a right-sided empyema might occur by direct extension from hepatic suppuration; while abscesses in distant portions of the body would suggest the carrying of the infection by the blood current.

Empyema occurred in the case described by Osler, and in the one herewith reported. Serous pleuritis was present in the cases reported

by Lannois and by Gerhard. In none of these cases did the hepatic suppuration indicate infection by the arterial supply.

Suppuration in distant portions of the body occurred in the cases described by Louis, suppuration in the parotid gland; by Chvostek, suppurative perichondritis; by Sidlo, pus in the mastoid, temple, and right axilla.

Very little can be found relating to urine, blood, and stool examinations in the reports of these cases. The findings in the case herewith described have been given.

Examination of the contents of the abscess cavities revealed pus of a light color in all cases except in those in which secondary pyosepticæmic abscesses were found. In these the pus was of a dark color. In cases where bacteriological examinations were made the colon bacillus was found. Lannois found the typhoid bacillus also in his case. A micrococcus was found by Dunin, and a staphylococcus was found in Romberg's case.

The symptoms in cases of abscess of the liver following typhoid fever extend over a variable period of time. Gerhard's case died on the fifty-fifth day; Romberg's on the thirty-second day, and the one that I described on the one hundred and first day. Most of the cases died from exhaustion. Dunin's case terminated suddenly. Osler's succumbed to peritonitis. Occasionally cases recover. Sidlo's case passed pus in the stools on the eighty-fourth day and was well on the one hundred and twenty-eighth day. Koht's case had, on the eightieth day, twenty bowel movements containing pus, and recovered on the one hundred and twentieth day. The cases that recovered were doubtless, from their histories, liver abscesses following pylephlebitis. French states that suppurative pylephlebitis may terminate in recovery. Treves[25] has operated on a case of suppurative pylephlebitis that recovered. I cannot find records of a case of hepatic abscess of arterial origin that got well. The prognosis in cases of hepatic suppuration following typhoid fever is always grave, and death may be expected in all cases associated with foci of suppuration in other portions of the body.

The diagnosis may be easy, difficult, or impossible. In Dunin's case the patient died suddenly without any symptoms indicating hepatic involvement. Pain in the hepatic region, chills, and enlargement and tenderness of the liver would suggest hepatic suppuration. Pylephlebitis might produce the same symptoms as hepatic abscess, and cannot be distinguished from it. Aspiration of the liver should be used as diagnostic aid.

The treatment of hepatic suppuration following typhoid fever is surgical. In all cases where a solitary abscess can be diagnosed, the pus should be evacuated by operation. Surgical interference is advised

against in cases of multiple abscesses of the liver. However, I believe that hepatic drainage would relieve the patient somewhat, and might be of value in some cases.

Case I.—(Lannois, *Revue de Médecine*, 1895, p. 913). The patient was in bed with typhoid for five or six weeks. After the temperature had been normal for three days, he had chills and fever, and ten days later had pain in the liver and stomach. These symptoms continued. The urine contained albumin. He became emaciated and died without being jaundiced or without the liver becoming enlarged.

Autopsy. The liver weighed 1800 grammes. Twelve abscesses containing yellow pus were found in the hepatic substance. Peritonitis was present. Thrombi were found in the mesenteric and portal veins and in the spleen. Peyer's patches were found in the stages of ulceration, healing, and pigmentation. The appendix was adherent, and one ulcer was found in its lumen. The biliary apparatus was normal. Right serofibrinous pleuritis was present. Typhoid and colon bacilli were found in the hepatic abscesses.

Case II.—(Osler, *Transactions of the Association of American Physicians*, 1897, vol. xii.). A man, aged thirty-seven years, suffered from septic symptoms. Three months previously he had had typhoid. Death resulted from peritonitis without symptoms of hepatic involvement.

Autopsy. Peritonitis. Appendix perforated. Pus in the mesentery. Empyema on the right side. The liver was large and contained many abscesses. Suppurative pylephlebitis was present. The splenic vein was thrombosed.

Case III.—(George S. Gerhard, *Medical News*, July, 1886). A man, aged twenty-six years, suffered from typhoid. On the twenty-first day the liver became large and tender and he suffered from diarrhœa. Chills developed and were accompanied by fever; later fluid appeared in the right pleural cavity. The patient declined rapidly. Fluctuation was found over the liver, and he died on the fifty-fifth day of his illness.

Autopsy. One large and many small abscesses were found in the liver. Fluid was present in the right pleural cavity. Peyer's patches were involved. The biliary apparatus seemed normal.

Case IV.—(Prof. Kohts, *Berliner klinische Wochenschrift*). A boy, aged eleven years, had typhoid. His temperature was normal on the thirtieth day. Two days later he had a chill, which was followed by pain in the liver, repeated chills and fever, jaundice, and hepatic enlargement. Eighty-four days after the onset of the illness he had a sudden pain in the abdomen followed by the passage of pus through the bowels. The patient recovered after being sick one hundred and twenty days.

Case V.—(Prof. Kohts, *loc. cit.*). A patient, aged twelve years, had the symptoms of typhoid. On the twenty-fifth day he had a chill which was followed by pain in the region of the liver. At the same time hepatic enlargement and tenderness over the entire abdomen became manifest. Death occurred on the thirty-first day of the illness.

Autopsy. The liver was enlarged and contained many abscesses. Thrombi were present in the portal vein. Suppuration was present in the mesentery. No abnormal changes were found in the biliary

apparatus; 100 grammes of fluid were found in the pericardial cavity. Peyer's patches were pigmented.

Case VI.—(Romberg, *Berliner klinische Wochenschrift*, March 3, 1890). A man, aged thirty-seven years, suffered from an ordinary attack of typhoid. On or about the eighteenth day of his illness he had a chill, which was followed by sweating, fever, pain in the liver, jaundice, enlargement of the liver, and tenderness over the hepatic and abdominal regions. His spleen was palpable. These symptoms progressed rapidly, and he died on the thirty-fourth day of his illness.

Autopsy. The liver was enlarged and contained many abscesses. Thrombi were found in the portal vein and in the hepatic artery. Peyer's patches were involved. Pus was found in the mesentery of the cæcum. Pneumonia was present, involving the lower lobe of the right lung. A staphylococcus was found in the hepatic abscesses.

Case VII.—(Louis, *Fievre Typhoide*, 1841, vol. i., obs. xvii.). The patient suffered from an ordinary attack of typhoid fever. During the decline of the fever he developed chills, fever, enlargement and tenderness of the liver, and jaundice. The patient died shortly after the appearance of these symptoms.

Autopsy. The liver was enlarged and contained one large abscess and six smaller ones. Peyer's patches were involved. Pus was found in the glands of the mesentery and in the parotid gland.

Case VIII.—(Chvostek, *Med. Chirurg. Rundschau*, June, 1868, p. 1888). This was an ordinary case of typhoid fever that developed septic symptoms, with pain and tenderness in the liver, accompanied by cough and expectoration. Jaundice was present. The patient died from exhaustion.

Autopsy. The liver was found enlarged and contained two large abscesses. The intestines showed evidences of typhoid infection. An abscess was found in the lung. Pericarditis was present.

Case IX.—(Burger, *Lancet*, October 17, 1874). This case differed clinically from the preceding one, in that no hepatic enlargement was present. The patient was jaundiced.

Autopsy. The liver was not enlarged, but many small abscesses were found in the right and left hepatic lobes. No other foci of suppuration were found. The portal vein was thrombosed. Peyer's patches showed evidences of recent involvement.

Case X.—(Sidlo, *Der Militar Aerzt*, Wien, 1875, No. 23, p. 20). This case of typhoid ran an ordinary course until the twenty-third day. Then he had chills, fever, and sweats, with pain and tenderness in the hepatic region, and with enlargement of the liver. He became jaundiced on the thirty-ninth day. Later, abscesses developed in the mastoid, temple, and right axilla. On the eighty-fourth day he developed a diarrhœa, and pus was passed through the bowels. The patient was well on the one hundred and twenty-eighth day.

Case XI.—(Petrini, *Prag. med. Wochen.*, 1888, Nos. 41 and 43). This case of typhoid developed chills and fever, with pain and tenderness in the liver; jaundice and hepatic enlargement on the thirteenth day of his illness. He died from exhaustion.

Autopsy. The liver was large and contained many small abscesses. Thrombi were present in the portal vein. The intestines showed typhoid lesions. No foci of suppuration were found in the body outside of the liver.

CASE XII.—(Theodore Dunin, *Deutsche Arch. für klin. Med.*, 1886, Band xxxix., p. 379). A patient, aged thirty-five years, complained of typhoid symptoms and also of a thenar inflammation. The suppuration in the hand opened spontaneously on the fourteenth day of his illness. The typhoid symptoms continued. The patient had no chills; neither did he complain of symptoms that would suggest involvement of the liver. No jaundice or hepatic enlargement were present. On the eighteenth day he got out of bed (was not delirious) to go to the lavatory, and died suddenly.

Autopsy. The liver was not enlarged. It contained many small abscesses. Suppurative pylephlebitis was present. The spleen was markedly enlarged, but no abscesses were found in it. Peyer's patches and the solitary follicles were infiltrated and necrotic. Œdema was present in the lower part of the right lung. The brain was anæmic. A micrococcus and an unidentified bacillus were found in the pus in the liver. No streptococci were present.

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A PRELIMINARY COMMUNICATION CONCERNING THE NATURE AND TREATMENT OF RECURRENT VOMITING IN CHILDREN.

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THE nature of the disorder that various authors have called recurrent, periodical, or cyclic vomiting has never been demonstrated, and the treatment has been correspondingly ineffectual. The commonest

theories as to its causation are that it is a neurosis, or that it is due to the so-called gouty or uric acid diathesis. The latter theory apparently has no better basis than the fact that the subjects of the disorder are members of families in which nutritional disturbances are common; while the term neurosis offers no substantial aid in coming to an understanding of the condition.

The observations that I shall report in this article are sufficient to show that in the individual cases to be mentioned there was, at the time of the attacks, but not in the intervals, a severe acid intoxication of the type seen in diabetes mellitus, and occasionally in other conditions. Treatment directed toward this acid intoxication has, in all but one of these cases, been strikingly successful; in the remaining case the result is still in doubt. These facts indicate that a cryptogenic acid intoxication is probably, in many cases, an important, perhaps the most important, element in producing the exhausting and occasionally fatal vomiting. If this proves to be true, proper treatment should often be successful in controlling or preventing the attacks.

The present conception of the importance of intoxication with acids that are produced in the organism has been arrived at chiefly through studies of the intoxication that occurs in diabetes mellitus, and that often leads to fatal coma. It has, however, been definitely shown that this form of intoxication is not confined to diabetes mellitus, but is sometimes seen in other conditions, such as carcinoma, grave anæmia, infectious diseases, and gastro-intestinal disturbances. When recognizable organic disease that is capable of causing acid intoxication is absent, the intoxication is called simply cryptogenic, or acid intoxication *sui generis*. I have recently discussed this condition,[1] and shall now refer to but a few important facts concerning it.

The symptoms that result from acid intoxication may be extremely varied. The most striking symptom that may appear is coma, with the peculiar type of respiration characteristic of this condition; but the intoxication may manifest itself in numerous other symptoms. In the type almost always seen (that in which beta-oybutyric acid is the chief acid present) the characteristic evidences of its existence are the odor of acetone to the breath, and particularly the presence of acetone, diacetic acid, and oxybutyric acid in the urine. The amounts of these substances found, especially of the latter, vary directly with the severity of the intoxication.

It was once thought that acetone produces the symptoms through its specific toxic effects. As is well known, this view has, however, been abandoned long since. It is now believed, on the basis of clinical observation and of animal experimentation, that no specific toxic agent

[1] Phila. Med. Journ., June, 1902.

is at work; but that the symptoms are due merely to the presence of an excessive amount of acids, and are produced by the reduction of the alkalinity of the tissues and of the body fluids, and the loss of alkalies in the excretions, the acids carrying the alkalies off in combination with them. The rational treatment of the condition is, therefore, to administer alkalies in extremely large doses, in order to neutralize artificially the excess of acids present.

Acetonuria has several times been noted in cases of recurrent vomiting. This seemed, however, from the reports to be of little consequence, as acetone and other evidences of acid intoxication frequently appear in the urine, as the result of inanition of any kind, and prolonged vomiting and abstinence from food are sufficient to cause acetonuria or diaceturia. Under such circumstances, the acid intoxication would be purely secondary and would have no importance as a primary factor in the production of the attack.

My interest in acid intoxication as a possible factor in exciting the attacks of recurrent vomiting was aroused by a case seen in January, 1901, the child of a relative from the West. In this case, the attacks had occurred frequently, in spite of rigid dieting and great care of the general health. They showed no definite relation to preliminary digestive disturbances, but were rather closely connected with excitement and overexertion. They had been increasing in frequency, but at the time I saw the child were somewhat less severe than they had been.

In the attack that I observed, the child exhibited, when seen a few hours after the onset of the vomiting, a very marked odor of acetone. This indicated that some degree of acid intoxication was present at the beginning of this attack, and that it might have something to do with producing the symptoms. I was unable to secure urine for examination, but ordered 20 grains of bicarbonate of soda to be given every two hours. The child retained this perfectly; and after four or five doses the vomiting and nausea stopped, and the patient rapidly recovered from the attack.

I then ordered large doses of bicarbonate of soda to be administered at once, if prodromal symptoms should appear at any time; and asked for a specimen of urine at the beginning of an attack if an attack occurred while the child was in this region. No attack has occurred at any time, however. Any suggestive symptoms have at once been treated with alkali, and the child has entirely escaped anything resembling the old attacks.

This case was mentioned in discussion at the meeting of the American Pediatric Society in June, 1902; and my further knowledge of the condition of the urine in these attacks and of the effect of large doses of alkalies is due chiefly to the kindness of Dr. Edward L. Pierson, of Salem, Massachusetts, who communicated with me soon there-

after concerning a case of recurrent vomiting in which he had been closely interested.

In this case, severe attacks, lasting for about a week and causing pronounced exhaustion, had occurred throughout a period of about eighteen months, and had been increasing in frequency. The child's health in the intervals was also growing decidedly unsatisfactory. I suggested examination of the urine for acetone and diacetic acid, and, if these should be found, the use of large amounts of alkali. The urine was first examined on the day of the onset of a typical attack, and both acetone and diacetic acid were found present. Alkalies were administered, and the attack ceased within thirty-six hours. The duration of this attack was about two days and a half, while the customary duration had been six or seven days.

Since that time this child's urine has been almost constantly watched for acetone and diacetic acid; and they have been found to appear together with the prodromal symptoms that had regularly preceded the previous attacks. In each instance except one the immediate use of large amounts of bicarbonate of soda (125 grains in divided doses) has prevented the apparently imminent attack; and in the instance in which this failed, Dr. Pierson believes that the alkali was not given sufficiently early. In a period of about nine months, then, this boy has had only one marked attack besides the one apparently abortive attack at the beginning of the treatment, and his general health has markedly improved.

Dr. Pierson also writes me that he has looked for acetone and diacetic acid in three other cases that he has had under observation, and that he has found these substances present in each case at the beginning of the attack. In all these cases alkalies were administered in the doses mentioned, and in all instances the treatment has been successful in aborting the attacks when used very early.

Dr. Pierson also states that in a further case, not his own, in which he had no opportunity to examine the urine, he suggested this treatment; and that it was used with success. He will himself report these cases in detail; and I shall mention only that he has regularly observed that preceding the attacks there are likely to be either excessive variations in or elevations of the temperature, which are not present when the child is entirely well. He consequently has the temperature taken twice daily, even when the child seems entirely well. If any prodromal symptoms appear, and particularly if the temperature begins to show distinct elevations, he has alkalies administered at once in large doses. He believes that the alkalies do not wholly abort the attack unless they are given before the vomiting has appeared, but considers that they may be depended upon in the cases that he has observed, if given sufficiently early.

I have not been fortunate enough to observe any typical cases since seeing the first one mentioned; nor have a number of pediatrists in Philadelphia who have kindly been watching for cases for me to examine. Recently, however, I have had opportunity to examine the urine of a typical case, subject to very frequent attacks, under the care of Dr. W. T. Sharpless, of West Chester, Pennsylvania. The urine was obtained during the first few hours of an attack. It contained acetone and diacetic acid in large amounts, the acetone being tested for in the distillate, and the diacetic acid test being controlled by boiling and also by extracting with ether. A test for oxybutyric acid by Külz's crotonic acid method yielded very large numbers of crystals in the distillate. The melting point of these crystals, after they had been washed with water and extracted with ether, was determined, and was found in two determinations to be between 71° and 72° C. Oxybutyric acid was evidently present, therefore, in large amounts.

Dr. Sharpless tells me that Mr. John D. Carter, of Haverford College, had twice tested the child's urine for acetone and diacetic acid at the time of an attack; and that he had found these substances present on both occasions. He also found them once in an interval; whether this was near the time of an attack or not was not noted. I had myself once before tested the urine during an interval, and had found it negative.

Dr. Sharpless instituted treatment in this case immediately after my last examination, a drachm of bicarbonate of soda being given three times a day. The attacks of vomiting had subsided when the alkali treatment was instituted, but the child had not become entirely well. After these large doses had been given for about a week the child vomited several times, and this was at first thought to be a mild attack of the usual kind. The vomiting occurred repeatedly at short intervals, however, and Dr. Sharpless concluded that the very large doses of soda were causing local irritation and reduced the dose, giving only enough alkali to keep the urine neutral. Since then, about a month, the child has had no vomiting and is improving in general health. It is, however, too early to decide as to the effect of the treatment.

The facts that I have mentioned concerning the condition of the urine and the effect of treatment demonstrate the presence of a marked acid intoxication in five cases; and probably, also, in the sixth case, mentioned by Dr. Pierson, but not seen by him. The effect of treatment in all the cases, excluding, as yet, that of Dr. Sharpless, makes it seem practically clear that acid intoxication was the chief factor in producing the violent vomiting; and the results of the treatment in five of the six cases have been altogether satisfactory, both to the medical attendants and to the parents, while previously entirely discouraging. I believe that it is probable that similar conditions will be found in at

least a considerable proportion of other cases; and, since other treatment has been extremely unsatisfactory, it is well worth while to try the effect of very large doses of alkali, even if acetone and diacetic acid are not known to be present, but particularly if they are found.

The cause of this acid intoxication can, of course, be only suspected; indeed, we do not definitely know the cause of acid intoxication in any condition. It is highly probable, however, that acidosis is of two varieties: one that is primarily due to a disturbance of metabolism; another that is due primarily to digestive disturbances, but that is perhaps intensified by secondary disturbances of metabolism. It seems very likely that in many cases of recurrent vomiting, and perhaps in all that show acid intoxication, the primary disturbance lies in the digestive tract. I have been unable, as yet, to carry out any studies that might throw light upon this question, as I have not had sufficient control of any case since the activity of acid intoxication in this disorder has come to seem of importance to me. I have, however, studies of this kind in operation, and shall attempt later on to give a broader and more detailed discussion of this question. For the present I may repeat what I have previously said (loc. cit.): that the evidences of acid intoxication have been found in a number of kinds of primary disease and under the guise of a variety of symptoms; that it is a simple matter to look for it; and if found in severe degree it should be treated. Heretofore, in conditions other than diabetes mellitus, interest seems to have been confined to demonstrating its occurrence. In the case of coma that I reported the man recovered from a condition that was desperately grave after enormous doses of alkali had been given intravenously; largely, I believe, as the result of the use of the alkali. In another case, under the care of Dr. S. M. Hamill—a child subject to recurrent attacks of gastro-intestinal disturbance associated with the passage of intestinal sand and not of the type of recurrent vomiting—I recently found the urine during an attack to contain large amounts of acetone, diacetic acid, and oxybutyric acid (crotonic acid test), and the administration of large doses of alkali caused a surprisingly rapid disappearance of the symptoms, while they had been extremely rebellious to other treatment.

Some observations that are in the main practically identical with those presented in this article, but which are not considered by their author in the same light, have been brought to my attention by Dr. J. P. Crozer Griffith. Marfan[1] describes a disorder that is probably identical with the recurrent vomiting of American authors. He states that he has regularly found acetone in the urine in the *beginning* of these attacks. He, however, attributes the condition to "acetonæmia."

[1] Arch. de Méd. des Enfants, 1901.

He doubts the correctness of the modern view that acetonuria indicates acid intoxication, considering that the meaning of acetonuria is wholly in doubt. He prefers to call the condition described by him "vomiting with acetonæmia."

These observations are, I believe, confirmatory of my view that acid intoxication exists in this disorder, for Marfan's interpretation of the observations is certainly incorrect. It has been well established that acetone is not the cause of the toxic symptoms in the form of intoxication in which it appears; that acid intoxication is present in cases associated with acetonuria; that it causes severe toxic symptoms; and that many of the toxic symptoms may be overcome or controlled for a long time, even in diabetes mellitus, if treatment with alkalies is begun early enough. It is even extremely questionable whether "acetonæmia" ever occurs, for it is at present doubtful whether acetone is ever excreted as such or appears only after the excretions leave the body as the result of oxidation of diacetic acid. Marfan rather unwillingly admits that acid intoxication may have something to do with the condition, and he consequently administers milk of magnesia in doses of "two centigrammes." This is probably a printer's error for two decigrammes; but the latter amount—about three grains—would be utterly ineffectual, even though it were absorbed, in case acid intoxication were present. Indeed, it would take but a very little gastric juice to neutralize such amounts. If this treatment is to be used at all some readily diffusible alkali, such as sodium bicarbonate or citrate, should be chosen, and extremely large doses should be given as soon as the first suggestion of an attack is observed; 100 grains, given as rapidly as possible, is probably a low limit. It is best to keep up the rapid administration of large doses until the urine is decidedly alkaline and then keep the urine alkaline until the symptoms have disappeared; and frequent moderately large doses would certainly be better than the occasional use of extremely large doses. During the interval one should give enough alkali to keep the urine about neutral. The doses of alkali commonly employed for other conditions will not demonstrate whether the treatment is effectual or not.

I wish it to be clearly understood that I am prepared to find that recurrent vomiting is not always due to acid intoxication: It is highly probable that the attacks that we call recurrent vomiting are not always dependent upon the same primary disorder. It will, however, be an easy matter to determine in how many cases this form of intoxication is present, and how frequently flooding the organs with alkalies will prove to be an effectual treatment.

UNILATERAL RENAL HÆMATURIA.[1]

By Augustus A. Eshner, M.D.,

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Blood may appear in the urine from various causes, some local, others general in operation. Among the former are congestion, inflammation, embolism, thrombosis, traumatism, retention, parasites, calculi or sand, tuberculosis, and new-growths, involving any portion of the urinary tract. The general causes for hæmaturia include certain infectious diseases, such as variola, measles, scarlet fever, typhoid fever, yellow fever, malarial fever, plague, and pneumonia; certain blood diseases, such as hæmophilia, scurvy, purpura, and leukæmia; certain forms of intoxication, such as that due to cantharides, to turpentine, to mercury, and to quinine, as well as intense jaundice. Hæmaturia has been observed also in cases of hysteria, in association with pregnancy and lactation, and in the sequence of violent physical exertion, and of sexual excess. Occasionally the cause of the condition is not obvious, and under such circumstances it has been variously described as essential or idiopathic hæmaturia, hæmaturia without lesion, hæmaturic nephralgia, renal hæmophilia, local hæmophilia, hæmophilic hæmaturia, angioneurotic hæmaturia. Cases of this sort, however, have become progressively less frequent in proportion as careful anatomical study is undertaken. In some instances the symptoms have pointed to involvement of one kidney; in a number the blood has been seen with the aid of cystoscopy, or of ureteral catheterization, or of direct inspection after cystotomy escaping from the corresponding ureter; and in many relief has followed operation on the kidney—sometimes simple manipulation, at other times nephropexy, at still other times nephrotomy, and at yet other times nephrectomy. Not rarely the kidney has appeared normal, even on section, but often more careful scrutiny has disclosed some abnormal condition, such as displacement or mobility of the kidney, obstruction of the ureter, the existence of pregnancy, the presence of calculi or sand, of tuberculosis, of neoplasm, or of the lesions of chronic nephritis.

I wish to report a case presenting symptoms of renal calculus, with hæmaturia, in which, after the kidney was exposed, found apparently healthy and left undisturbed, the symptoms disappeared permanently.

A girl, twenty years old, employed as a sewing-machine operator in a shirt factory, presented herself on account of constant pain in the

[1] Read before the Medical Society of the State of Pennsylvania, September, 1902.

right side of the abdomen, radiating to the right lower extremity and sometimes over the entire abdomen, with acute paroxysmal exacerbations persisting for from ten days to two weeks, and then gradually subsiding. During the exacerbations the urine assumed a red color supposed to be due to the presence of blood. These symptoms had been present for twelve years, since the age of eight. Urination was not increased in frequency, and was attended with mitigation of the pain. The appetite was impaired, but the pain was uninfluenced by the ingestion of food. There was no vomiting and the bowels acted regularly. There was freedom from cough, expectoration, and œdema. Sleep was not disturbed. The patient complained of frontal headache and of pain in the chest and in the left lower extremity. Menstruation began at thirteen, and had always been regular and unattended with pain, but was profuse. There had been slight loss in weight, but no undue perspiration. The patient, however, appeared well-nourished and her color was good. There was nothing noteworthy in the family history or in the past personal history. The urine presented a red color, an acid reaction and a specific gravity of 1022. It contained a considerable amount of albumin, but no sugar. On microscopic examination a large number of red blood corpuscles were found, together with a moderate number of epithelial cells, a few leucocytes, many crystals of calcium oxalate and granular tube casts. The condition was looked upon as one of renal calculus, and the patient was admitted to the Polyclinic Hospital. The urine at this time was at first bloody, but subsequently it became clear, although microscopic examination continued to disclose the presence of red blood cells.

Dr. L. W. Steinbach, who saw the case in consultation with me, concurred in the diagnosis, and accordingly the right kidney was exposed, but nothing abnormal was found in this organ or the surrounding tissues. The organ was replaced, and surgical recovery was uneventful. The urine was bloody for a short time after the operation, and on several occasions the patient passed a number of somewhat ovoid concretions, the largest of which was 5 mm. in the long and 3 mm. in the short diameter. These were dark red in color and smooth on the surface, some presenting a dull and others a lustrous appearance. They floated on the surface of water, in which, however, they failed to dissolve. They were insoluble also in acids and in alcohol. On microscopic and chemical examination they were found to contain, in addition to red blood corpuscles, crystals of calcium oxalate, phosphates, cystin, and other substances not yielding the reactions for uric acid. Examination of the blood after the operation showed the hæmoglobin percentage to be 78, the number of red blood corpuscles 4,316,000, and the number of leucocytes 9000 in the cubic millimetre. Pain in the right loin persisted for a considerable time, and micturition was attended with burning, but the urine shortly became free from abnormal content, and the patient stated that she felt better than she had at any time in the previous ten years. There had been no recurrence of the hæmaturia a year after the operation, and more than a year has elapsed since the last report.

I have seen the patient within a few days, and while there has been no return of the hæmaturia, micturition is reported to be attended with a sense of burning, and a precipitate is said to be deposited from the urine. Some of the latter brought to me presents a whitish pulveru-

lent and granular appearance, is hard and gritty to the touch, and does not dissolve readily in water. On microscopic examination it is found to consist of granular matter without crystalline form.

Briefly summarized, we have here a case in which the recurrent hæmaturia, with paroxysmal exacerbations of pain in the right loin, extending over a long period of time, without marked wasting or cachexia or evidence of other disease, seemed to point clearly to the presence of a calculus in the right kidney or its pelvis. Operation, however, with exposure and manipulation, though without incision, of the suspected organ failed to disclose the presence of a foreign body or of any other abnormality. The presence of albumin, tube casts, and crystals of oxalates in the urine prior to operation suggests the existence of irritation or inflammation of the kidney, while the small concretions that were discharged after the operation, and consisting principally of blood clot, although they contained other matters, would seem to have been a result rather than the cause of the bleeding. Although the evidence is not conclusive, it is safe to assume that the blood came from the right kidney alone. This view is sustained by the cessation of the hæmaturia after exposure and manipulation of this organ, although no underlying cause was discovered, and, therefore, nothing further was undertaken with the definite object of effecting its removal. It may be conceived that as a result of the necessary operative manipulations fine sand-like particles or minute calculi were dislodged, and thus a source of irritation removed, or that certain changes were thereby brought about in the circulatory conditions of the kidney, but neither of these explanations is entirely satisfactory. The long duration and the subsequent recovery militate against malignant disease and tuberculosis, and there was no indication of hæmophilia. The case must, therefore, be looked upon as an example of hemorrhage from one kidney of obscure origin, with cessation of the hæmaturia in the sequence of surgical intervention involving only exposure and manipulation of the suspected organ.

I have succeeded in collecting from the literature a number of cases of similar or related character.

The *British Medical Journal* for May 18, 1872, pp. 534 and 565, contains references to an operation undertaken by Mr. Durham upon a woman, aged forty-three years, with the expectation of finding a calculus in or about the pelvis of the right kidney. No calculus being found, and the kidney appearing healthy, the organ was returned and the wound closed. Pain, hæmaturia, and other symptoms, however, persisting for more than two years after the operation, nephrectomy was performed, but the patient died a short time afterward.

C. Lauenstein[1] relates the case of a sailor, forty-seven years old,

[1] Deutsche medicinische Wochenschrift, June 30, 1887, p. 56.

who for twelve years suffered from constant pain in the right loin, with paroxysmal exacerbations and profuse hæmaturia. The urine contained red and white blood corpuscles and crystals of lime salts. The right kidney was exposed, its pelvis opened, puncture made in three places, but nothing abnormal was detected. The urine became clear in the course of a few days and remained so.

William Anderson[1] reports the case of a woman, twenty-four years old, who for four years had had recurrent attacks of hæmaturia, with pain in the right loin and groin. Renal calculus being suspected the right kidney was exposed, palpated, and punctured, but no abnormality was found. The patient was better for a time, but the symptoms returned in the course of a month, although permanent improvement subsequently ensued. The case was considered an example of some complicated form of neurosis.

Under the designation of hæmaturic nephralgia, A. Sabatier[2] has reported the case of a woman, thirty years old, who for seven or eight years had had attacks of oppression, with œdema of the lower extremities, especially on the right side, and a painful swelling in the right flank. The urine was at first chocolate colored and contained blood, but no tubercle bacilli. Later there developed headache, vomiting, nausea, and pain in the right flank. On palpation over the right kidney pain was induced, but no tumor could be distinguished. The urine was now scanty and bloody. An attack of uræmia occurred and was relieved by bleeding. The hæmaturia became gradually more marked, clots at times appearing in the urine, but the general health remained good. The pain in the right loin increased to such a degree as to prevent recumbency on that side. It was induced by walking and by inclination of the body to the right side, and it radiated in paroxysms to the ureter, the bladder and the lower extremities. The symptoms were thought to be due to calculous pyelitis, the stone occluding the ureter from time to time. Accordingly, operation was decided upon and the kidney was exposed through a lumbar incision and divided down to its pelvis, but no stone or neoplasm was discovered, although a sound was introduced into the ureter. On account of the profuse hemorrhage, and with a view of causing obliteration of the ureter in case that structure was the seat of the lesion, the kidney was removed. The patient made a speedy recovery, and the hemorrhage had not recurred two years after operation. Examination of the removed organ disclosed no abnormality.

M. Schede[3] has reported the case of a robust man, fifty years old, without hereditary predisposition, in whom hæmaturia appeared in the sequence of the ingestion of a cold drink. There was at first a sense of coldness in the left lumbar region, and later transient pain of moderate severity in this situation and in the bladder. The bleeding recurred when the patient assumed the erect posture and ceased in the recumbent posture. It grew progressively more marked until it could no longer be prevented by even the most absolute rest. The patient had been kept in bed for four weeks, but the urine had been continuously bloody for one week. The general condition had not suffered greatly, although there was slight wasting. There was no fever.

[1] Lancet, April 20, 1889.
[2] Revue de Chirurgie, 1889, ix. p. 62.
[3] Jahrbuch der Hamburger Staatskrankenanstalten, I. Jahrgang, 1889, p. 235.

Neither kidney could be made out on palpation, and nothing abnormal was found on examination of the bladder with the aid of the sound and the endoscope. The urine contained red and white blood corpuscles and ciliated epithelial cells. Styptics were administered, but without relief. Three possibilities were considered: 1. A calculus in the pelvis of the kidney causing erosion of the bloodvessel. 2. Primary miliary tuberculosis. 3. Beginning malignant disease.

On account of the persistence of the hemorrhage operation was decided upon, and in order to determine if possible which kidney was the seat of the disease suprapubic cystotomy was performed, and each ureter catheterized. By this means it was learned that the blood came from the left kidney. Accordingly, this organ was exposed, but it was found normal in form and size, and neither stone nor tumor could be detected, even after incision of the renal pelvis. It was decided that in order to prevent further hemorrhage it would be best to remove the kidney, and this was done. The wound united without complication and the hæmaturia was not repeated. The removed kidney was found to be friable and anæmic, and the seat of small petechiæ. Microscopic examination disclosed the presence of isolated, almost disintegrated tube casts, covered with red blood corpuscles.

Schede suggests the name of local hæmophilia for the condition, but it seems not impossible that the kidney was the seat of an inflammatory process.

Under the title of renal hæmophilia, H. Senator[1] describes a case of hæmaturia of two and one-quarter years' standing in a girl, nineteen years old. At first the urine was discolored in connection with menstruation, and at this time it contained only hæmoglobin, but no red blood corpuscles. Later red blood corpuscles made their appearance, and the hæmaturia occurred independently of menstruation and without pain. There was slight increase in the frequency of micturition, but no bearing down or tenesmus. Anæmia and slight cough suggested the possibility of tuberculosis, but there was no fever and little wasting.

The case was looked upon as one of hæmophilia, as the patient had four brothers and sisters who exhibited a marked tendency to epistaxis, while the father had from youth suffered from the same condition and also from hæmoptysis without evidence of disease of the lungs, and eleven of his brothers and sisters, as well as other and more distant relatives also suffered from epistaxis, and among the women profuse menstruation was common.

Physical examination failed to disclose any evidence of visceral disease, while with the aid of the cystoscope blood could be seen entering the bladder from the right ureter. As the patient was growing progressively worse, and in order to avert a fatal issue, the right kidney was removed. The urine was bloody for a day or two after the operation, but thereafter it became and remained clear. The wound healed without complication, and the patient was dismissed as well after four weeks. On microscopic examination extravasations of blood were

[1] Verhandlungen der Berliner medicinischen Gesellschaft aus dem Gesellschaftsjahre, 1890; Separat-abdruck aus der Berliner klinischen Wochenschrift, 1891, B. xxi. p. 293.

found in the removed organ, and lesions of slight circumscribed interstitial nephritis—a condition thought to be characteristic of hæmophilia. Senator considers hæmophilia a congenital hereditary tendency to hemorrhage, which may be local as well as general.

This case must be considered as one of nephritis rather than one of hæmophilia in the strict sense of the word, as the patient herself exhibited no undue tendency to hemorrhage apart from the hæmaturia, and the histological examination revealed the lesions of the former condition.

Robert Abbe[1] exhibited to the Section on General Surgery of the New York Academy of Medicine a patient who, five years previously, had begun to suffer from renal colic and hæmaturia, which continued for two years. The hemorrhage had recurred within six weeks, and cystoscopic examination showed that the blood came from the right ureter. The right kidney was exposed and found normal. It was stripped of its capsule and fifteen punctures made at different places on the convexity of the organ. At one point only was any sense of abnormality appreciated. In this situation the kidney was incised and a finger introduced into the pelvis of the organ. No stone was found, but the finger came in contact with a gritty point, which it was thought might have corresponded to the papilla of one of the pyramids. The wound was closed without further intervention and the patient was thereafter free from pain and hæmaturia.

F. Legueu[2] reports the case of a man, twenty-six years old, with a neuropathic history, who suffered from recurrent attacks of pain in the left iliac region, generally attended with hæmaturia, and superinduced by exercise and coitus. On examination the left kidney was found to be tender and slightly increased in size. The organ was exposed and found slightly depressed and mobile. It was freed from its capsule and grasped between the fingers, but no abnormality was detected. Temporary relief followed, but death took place in the course of two months. The condition was looked upon as one of idiopathic renal neuralgia in a neuropathic subject.

Albert L. Stavely[3] reports two cases of hæmaturia in which the bleeding ceased in the sequence of an incision of the kidney from which ureteral catheterization showed the blood to be derived. One of the patients was a woman, thirty-nine years old, with a family history of tuberculosis and symptoms of the same disease, who for five years had had intermittent hæmaturia of increasing severity. The urine contained blood, but no tubercle bacilli could be found. Blood was obtained from the left ureter with the aid of a catheter. The bladder had to be incised to gain access to the right ureter. The former appeared healthy, while the urine from the latter contained a trace of blood. The left kidney was exposed and presented an area of doubtful fluctuation along its convex border, but when an incision was made down to the pelvis of the organ careful inspection failed to disclose

[1] Medical Record, May 16, 1891, p. 573.
[2] Annales des Maladies des Organes Genito-Urinaires, August, September, November, 1891.
[3] Bulletin of the Johns Hopkins Hospital, March, 1893, p. 25.

any disease. The hæmaturia ceased after a slight temporary recurrence.

The second case occurred in a woman, in whom the hæmaturia had set in suddenly and had persisted intermittently for a year, growing progressively worse. The urine contained a large amount of albumin, numerous red blood corpuscles, a few leucocytes, a few large epithelial cells, but no casts. On catheterization blood was obtained from the left ureter, while the urine from the right ureter was clear. The left kidney was exposed and incised, but it presented no macroscopic evidence of disease. Histological examination of a bit of removed tissue, however, disclosed lesions of chronic nephritis. The urine contained albumin and blood for a time after the operation, but both eventually disappeared.

J. Israel[1] reports the case of a previously healthy woman, forty-two years old, without hereditary predisposition, in whom three weeks following an attack attended with severe pain in the left chest and a chill, hæmaturia occurred and persisted for eleven days. Both kidneys were palpable, displaced downward, and apparently normal, the left being especially movable and tender. The urine contained red blood corpuscles and renal epithelium. On cystoscopic examination blood was seen escaping from the left ureter. On account of a possibility of the presence of a small tumor the kidney was exposed and incised freely, but no abnormality was found. The halves of the kidney were united by suture and the organ was replaced, and primary union took place. The hæmaturia continued freely for three days, but thereafter it began to subside. On the seventh day only traces of blood were present in the urine, on the eleventh day none whatever, and on the thirteenth day none could be detected microscopically. There was no recurrence of the hæmaturia and the patient remained well. Israel was inclined to attribute the favorable result in this case to the influence of the operation.

A. Broca[2] reports the case of a woman, twenty-eight years old, who had suffered from hæmaturia for sixteen months, together with dull pain in the loins, greater on the right. The urine contained blood, casts, crystals, but no tubercle bacilli. Tuberculosis or neoplasm was suspected, and accordingly the right kidney was exposed, its capsule removed and the organ carefully palpated, but no abnormality was found. The first micturition following the operation was bloody, but subsequently the urine was clear for at least three years.

L. Picque and Th. Reblaub[3] have reported the case of a woman, seventy-six years old, who had suffered from hæmaturia for four months. On examination the left loin was found the seat of pain on percussion, and a large body was appreciable on palpation. When viewed with the cystoscope the bladder appeared to contain a neoplasm, but this proved to be a collection of blood clot, and after its removal the hemorrhage ceased. The left kidney was, nevertheless, exposed, and on removal of its fatty capsule exhibited a voluminous cyst at its inferior pole. This was evacuated and its walls excised. No other lesion was found on careful palpation, and on section the kidney appeared

[1] Archiv für klinische Chirurgie, 1894, Bd. xlvii. p. 428.
[2] Annales des Maladies des Organes Genito-Urinaires, December, 1894, p. 881.
[3] Neuvième Congrès de Chirurgie, Paris, 1895, p. 580.

perfectly normal. The organ was returned to the abdominal cavity and perfect recovery ensued.

At a later date Picque[1] reported that hæmaturia returned after an interval of three years. Cystoscopic examination now disclosed the presence of a tumor in the bladder near the mouth of the right ureter. Suprapubic cystotomy was performed and the tumor removed. Recovery ensued.

Picque and Reblaub have reported also the case of a woman, thirty-nine years old, seen in the service of Professor Guyon, who had suffered from hæmaturia for eighteen months and from shooting pains in the right loin for seven months. On examination the right kidney seemed enlarged and mobile and slightly irregular on its surface, as well as tender. With the aid of the cystoscope blood was seen to escape from the right ureter on pressure over the right kidney. The urine contained a large number of red blood corpuscles and epithelial cells from the bladder, but no tubercle bacilli. The presence of a neoplasm being suspected the kidney was exposed, but no abnormality was found and the organ was replaced. The urine became clear on the day after the operation, and remained so thereafter.

Picque and Reblaub were inclined to look upon the hæmaturia as of vasomotor origin and comparable to the hæmoptysis and epistaxis observed in hysterical individuals.

Thomas Oliver[2] has related the case of a sailor presenting profuse hæmaturia, with pain in the left loin. The bladder being found normal on examination, the left kidney was exposed, probed, cut, and examined, but no stone was found. The organ was replaced, but the patient failed to rally. At autopsy no microscopic evidence of disease could be detected, but histological examination disclosed lesions of interstitial nephritis.

In another case cited by Oliver, a man, fifty-four years old, suffered from paroxysmal pain in the right loin, with hæmaturia. When the right kidney was exposed it was found greatly shrivelled, but no calculus could be detected with the aid of a needle. The hæmaturia ceased in the course of a few days, and there was no return during the remaining seven or eight years of the patient's life.

George Elb[3] reports the case of a man, twenty-two years old, who had two attacks of hæmaturia a year apart. On cystoscopic examination the blood was seen to come from the left ureter, while the urine from the right ureter was clear. The left kidney, when removed, presented no lesion, and there was no further return of the hæmaturia. This case is reported—as one of angioneurotic hæmaturia—also by G. Klemperer[4] in the course of a paper on "Hemorrhage from Healthy Kidneys," read before the Berlin Society for Internal Medicine. In the discussion of this communication Nitze[5] stated that he had operated upon seven cases of "essential hæmaturia," dividing the kidney in three and removing it in four. Recovery ensued in all.

F. Guyon[6] reports the case of a man, twenty-six years old, with a

[1] Bulletin et Mémoires de la Société de Chirurgie de Paris, 1898, vol. xxiv. p. 594.
[2] International Clinics, 1895, vol. iii. 5th series, p. 59.
[3] Inaugural Dissertation, Berlin, 1896.
[4] Deutsche medicinische Wochenschrift, February 25, March 4, 1897.
[5] Vereins-beilage der Deutschen medicinischen Wochenschrift, February 18, 1897, p. 54.
[6] Annales des Maladies des Organes Genito-Urinaires, February, 1897, p. 113.

history of malarial fever, who suffered from three attacks of hæmaturia in the course of nineteen months. On examination the right kidney appeared enlarged and irregular, and with the aid of the cystoscope blood could be seen coming from the right ureter. The urine was purulent and contained tubercle bacilli. On rectal examination nodules could be felt at the base of the prostate gland. The right kidney was thought to be tuberculous, and accordingly it was exposed and divided. In spite, however, of most careful search no lesion could be found and the organ was sutured and replaced.

Guyon reports also the case of a woman, thirty-five years old, who suffered from hæmaturia during her second and third pregnancies, with a recurrence while nursing the last child. There was pain in the right loin and the corresponding kidney appeared enlarged and irregular. Lactation was suspended and the hæmaturia ceased at once. The right kidney, being thought to be carcinomatous, was exposed, found normal, and replaced. There was no return of the bleeding. Guyon believed the hæmaturia to be the result of congestion of the kidney.

De Keersmaecker[1] reports the case of a woman, forty-three years old, who had suffered for many years from painful micturition, and for two years from hæmaturia in varying degree. The urine contained blood cells, but no tubercle bacilli or tube casts or renal elements. On cystoscopic examination the bladder was found normal, but the ureteral orifices could not be seen. A catheter was, however, introduced into each ureter and it was found that the blood came from the left kidney. As this organ appeared enlarged, it was exposed, found mobile, and removed. There was no subsequent return of the hæmaturia. The organ was found the seat of chronic nephritis.

Debaisieux[2] has reported the case of a woman, twenty years old, who for six months following an attack of influenza suffered from hæmaturia, with colicky pain in the left half of the abdomen, loin, and iliac fossa. The urine contained blood cells and a corresponding amount of albumin, but no casts or crystals. The presence of a calculus or a neoplasm being suspected, the kidney was exposed, incised, and examined, and two translucent prominences, as large as a pin-head, were detected on the mucous membrane of the renal pelvis. The urine became clear three days following the operation, and was still so two and one-half years later.

In discussing the report of this case, Dandois[3] related the case of a woman, thirty years old, suffering from hæmaturia of sudden onset, with colicky pain in the right loin. Nephrotomy was performed, and the kidney found only the seat of congestion. The bleeding and the pain ceased and did not return. The further course of the case proved that the patient had been pregnant for one week before the occurrence of the hæmaturia.

Gallet[4] referred to a case of mobile kidney with hæmaturia in which relief was afforded by nephropexy.

M. L. Harris[5] reports the case of a farmer, fifty years old, who had suffered from hæmaturia for three years. Cystoscopic examination showed that the blood came from the left ureter. The urine contained blood corpuscles and a small amount of albumin, but no tube casts.

[1] Annales de la Société Belge de Chirurgie, 1897, p. 159.
[2] Ibid., p. 205. [3] Ibid., p. 215. [4] Ibid., p. 219.
[5] Philadelphia Medical Journal, March 19, 1898, p. 508.

The condition was thought to depend upon an angioma of the renal pelvis or of the kidney itself, or to be one of angioneurotic hæmaturia. Medicinal treatment failing to yield relief, the kidney was exposed, but found normal in every respect. Nevertheless, the organ was divided, but no abnormality was found. The kidney was united and replaced, and the urine gradually became clear and remained so.

Genouville[1] reports the case of a man, fifty-one years old, who for a year suffered from attacks of pain in the right loin suggestive of renal colic, and the later of which were followed by hæmaturia. On cystoscopic examination the bladder presented a normal appearance, but blood was seen issuing from the right ureter. A diagnosis of calculus or neoplasm was made, but the corresponding kidney was exposed, found irregular on its surface, elongated, flattened, and empty. Removal of the renal capsule was readily effected, but bleeding followed. The kidney was divided and the parenchyma found of varying thickness, with some fragments of false membrane in the renal pelvis. The condition was looked upon as one of secondary hydronephrosis. At a later date nephrectomy was performed and there was no recurrence of the hæmaturia.

Genouville reports a second case, in a man, thirty-five years old, who suffered from hæmaturia, with pain at first in the left and later in the right loin. The urine at first contained little blood and no albumin, but later albumin and tube casts also were found present. The blood was observed to come from the right ureter, and the corresponding kidney was exposed and found large and hyperæmic. The organ was incised, but only capsular adhesions were found. There was no hæmaturia for a year and a half after the operation, but there was at this time for two or three days a copious admixture of blood with the urine, which again contained albumin and tube casts.

Genouville refers further to two cases of profuse hæmaturia with pain in the loin, the blood coming from the right kidney. When exposed the organ was found only mobile, no lesion being appreciable on incision. Relief followed nephropexy.

Demons[2] has reported the case of a woman, twenty-four years old, who had an attack of colicky pain in the left lumbar region and two years later copious persistent hæmaturia for a period of several weeks. On deep palpation the left kidney was found tender, but not enlarged or displaced. On cystoscopic examination blood was seen escaping from the left ureter. When the kidney was exposed subcapsular ecchymoses and cicatricial depressions came into view. The organ was incised, the cortical tissue found denser than normal, and the renal substance presented a yellowish tint. Nephrectomy was decided upon and performed and there was no return of the hæmaturia. Histological examination disclosed sclerotic changes involving especially the glomeruli and the collecting tubules.

Loumeau[3] has reported the case of a woman, thirty-two years old, subject to rheumatic pains and nasal and hemorrhoidal bleeding, who suffered at first from several slight attacks of hæmaturia under the influence of cold, and thirteen months later from persistent hæmaturia

[1] Annales des Maladies des Organes Genito-Urinaires, 1898, p. 449.
[2] XII. Congrès de Chirurgie, Paris, 1898, p. 408.
[3] Ibid., 1898, p. 413.

for a period of seven months, together with slight pain in the left groin and tenderness on palpation of this region. The urine was found free from tubercle bacilli. On cystoscopic examination blood was seen escaping from the left ureter. When exposed the kidney appeared congested and it was divided, but no lesion was apparent, and the organ was replaced. There had been no return of the hæmaturia at the time of report, four months after operation, and reference is made to the case also at a later date.[1]

Debersaques[2] reports the case of a fisherman, thirty-eight years old, who suffered for twenty years from pain in the left loin, for eight years from intermittent hæmaturia, and for three years from violent and paroxysmal pain in the left loin, inguinal region, and genitalia. Microscopic examination disclosed the presence of blood corpuscles in the urine. On palpation in narcosis the left kidney was found slightly mobile, and pressure caused slight pain. The organ was exposed and incised and found congested. A sound was introduced into the ureter, but no abnormality could be detected. The hæmaturia ceased after the first day following the operation.

Poirier[3] has reported the case of a woman, forty-eight years old, who for three months had suffered from hæmaturia, with rapid emaciation and general lassitude. The urine contained a considerable amount of albumin and a large number of red blood corpuscles. On cystoscopic examination pure blood could be seen escaping from the right ureter into the bladder. The presence of a renal calculus was suspected, and accordingly the kidney was exposed and incised. The organ was normal in size, lobulated, granular, and cystic, but no foreign body was found. Nephrectomy was performed. The urine contained much less albumin after the operation and no red blood corpuscles. On histological examination lesions of chronic nephritis were found. Three months later the patient was seized with symptoms of asthma and pulmonary congestion, and death resulted, it is supposed, in consequence of a lighting up of disease in the remaining kidney.

Pousson[4] has reported the case of a woman, twenty-three old years who for five months had had hæmaturia at progressively shorter intervals and in gradually increasing degree. On palpation the right kidney was found displaced and enlarged, but not painful. On cystoscopic examination the urine from the right ureter could be seen to be bloody. In addition to red and white blood corpuscles, it contained albumin and tube casts, but no tubercle bacilli. The condition was, nevertheless, thought to be dependent upon primary renal tuberculosis or upon epithelioma of the pelvis of the kidney. Accordingly the organ was exposed and divided down to its pelvis. The kidney presented an irregularly hyperæmic and anæmic appearance, and its removal was decided upon and effected. On histological examination there were found lesions of chronic nephritis. The hæmaturia did not recur, although the urine continued to contain a trace of albumin.

Potherat[5] has reported the case of a woman, fifty-two years old, who for eighteen months had been suffering from profuse hæmaturia,

[1] L'Association Française d'Urologie, Paris, 1900, p. 125.
[2] Annales de la Société Belge de Chirurgie, July, 1898.
[3] Bulletin et Mémoires de la Société de Chirurgie de Paris, 1898, xxiv. pp. 462, 593.
[4] Ibid., p. 590.
[5] Ibid., p. 634.

resulting in anæmia and compelling the patient to remain in bed. On examination the right kidney was found enlarged, displaced downward, and nodular. The urine contained albumin in small amount. The presence of a neoplasm being suspected, the kidney was exposed and removed. For four days after the operation the patient suffered from anuria. This was temporarily relieved, but it gradually returned and death resulted from uræmia. On histological examination the removed organ presented lesions of an inflammatory character, and the condition was considered one of chronic interstitial nephritis, the disease, however, being more pronounced on the left side.

T. Rovsing[1] reports four cases of hæmaturia in which the bleeding ceased in the sequence of nephrotomy. The first occurred in a woman, twenty-one years old, who from the age of sixteen had suffered from attacks of pain in the right side of the abdomen that were considered to be due to appendicitis, but with which later hæmaturia became associated. On cystoscopic examination blood was seen escaping from the right ureter. The urine contained blood corpuscles, but no tubercle bacilli or other bacteria. On making an incision in the right lumbar region the kidney was found adherent in its upper third and this presented a bluish-red appearance, as did also a section of the organ when divided from its convex border. No other abnormality was found. On the following day the urine was slightly mixed with blood, but on the third day it was quite clear, and from the eighth day it was entirely free from blood. There had been no recurrence of the hæmaturia in eighteen months. Microscopic examination of a bit of tissue removed from the kidney disclosed venous and capillary stasis, in places with small circumscribed areas of necrosis not cuneiform in shape, fresh thrombi in the straight arteries, extravasations of blood in Bowman's capsules, and hyaline casts in the convoluted tubules. The bleeding and the changes in the upper third of the kidney were thought to be due to compression of the organ between the liver and the ribs as a result of tight lacing, the operation freeing adhesions and releasing the organ.

The second case occurred in a woman, fifty-six years old, who, after hard work and heavy lifting, at the age of forty-four noticed the presence of blood in the urine. The hæmaturia was repeated ten years later and again sixteen days before coming under observation. The patient was pallid, emaciated, and cachectic-looking. In the right loin could be felt a large, hard tumor, which was thought to be the enlarged kidney. On cystoscopic examination blood could be seen escaping from the right ureter. The urine contained blood cells and bacterium coli. Through an incision in the right loin the kidney was found displaced downward and occupying an oblique position, with its upper pole directed toward the vertebral column and its convex border forward and upward. The organ was divided from its convex border and presented a cyanotic appearance. No other lesion was discovered and the two halves were sutured, the kidney replaced, and the wound closed. The urine was clear on the following day, and eleven days later it no longer yielded the chemical reactions for blood. After the lapse of six days more the bacterium coli was present, but at the end of two months the urine was sterile. On microscopic examination of

[1] British Medical Journal, November 19, 1898, p. 1547.

a bit of tissue removed from the kidney, venous and capillary stasis was found, with a number of bacilli in the straight tubes. In this case also the displacement of the kidney was attributed to tight lacing.

The third case occurred in a man, forty-seven years old, who had for three months been suffering from hæmaturia, with a dragging sensation in the left loin. Micturition was unattended with pain. The left epididymis was the seat of a flat, uneven infiltration. On cystoscopic examination blood was seen issuing from the left ureter. No tubercle bacilli or other bacteria and no crystals were found in the urine. A tumor or tuberculosis of the left kidney was suspected, but on exposure of this organ it was found situated high up under the diaphragm, but otherwise apparently normal in every respect, even after division. The right kidney also was found healthy. The urine contained blood for two days, but thereafter it was clear.

In this case it is suggested that there was possibly a small tuberculous focus that was overlooked, or some other lesion that underwent cure as a result of the incision.

The fourth case occurred in a woman, twenty-eight years old, who had suffered for four years from pain in the left loin following physical exertion. After a severe exacerbation, in which the pain radiated toward the bladder and was attended with frequent vesical tenesmus, hæmaturia set in and persisted for six days, although subsequently the urine did not become entirely clear. Renal calculus was suspected, but in the absence of a positive diagnosis operation was not undertaken. The patient grew worse, and the pain more severe, and the left kidney became enlarged and displaced. Cystoscopic examination now showed turbid, bloody urine issuing from the left ureter. The urine contained blood corpuscles, epithelial cells, and bacterium coli. On operation the left kidney was found displaced downward, its pelvis dilated and the ureter bent on itself. On division of the kidney turbid, bloody urine escaped. The renal pelvis was irrigated, the wound sutured, and the organ fixed in place. The urine was clear on the second day after the operation. Examination of a bit of tissue removed from the kidney showed this to be normal except for the presence of groups of bacteria in the straight tubes.

T. Myles[1] reports the case of a woman, twenty-six years old, who, shortly after a successful operation for the relief of hemorrhoids, was seized with recurrent attacks of dull, aching pain in the left side of the abdomen, occasionally attended with vomiting. Hæmaturia set in and was attended with progressive emaciation and anæmia. Both kidneys were movable, especially the left, and pressure over the latter caused suffering. The urine consisted of almost pure blood, and it contained no tubercle bacilli. On cystoscopic examination blood was seen escaping from the left ureter. Rest and styptics failing to control the hemorrhage, the left kidney was exposed and found enlarged, congested, and lobulated. The pelvis of the kidney was incised and a long, flexible, metallic bougie was introduced into the ureter. No obstruction was found, and the calices were examined with the finger and the sound, but nothing abnormal was detected. An exploring needle was plunged into the substance of the kidney in various situations, but no lesion discovered. The kidney was fixed in position and

[1] Medical Press and Circular, August 23, 1899, p. 179.

the wound closed, but the hæmaturia persisted. Accordingly the kidney was removed twenty-three days after the primary operation and the hemorrhage thereafter ceased. On histological examination diffuse myxangiomatous change was found in the submucous tissues of the pelvis of the kidney, while the tissues of the kidney were the seat of but slight changes.

E. Hurry Fenwick[1] states that he has in numerous instances observed painless unilateral renal hæmaturia in young persons, without the discovery on nephrotomy and digital exploration of the pelvis of the kidney of a cause for the hemorrhage. He reports two such cases in which when the kidney was opened and exposed to electric illumination a condition of papillary telangiectasis was found, and removal of which was followed by cessation of the hæmaturia.

The one patient was a woman, eighteen years old, who had suffered from intermittent hæmaturia of five years' standing, without the presence in the urine of tube casts, tubercle bacilli, or cells from the renal pelvis. The possibility of hysteria and of calculus was taken into consideration. On cystoscopic examination blood was seen entering the bladder from the left ureter. The corresponding kidney was accordingly exposed, but nothing abnormal was found until the pelvis of the kidney was opened, when, under electric illumination, a tuft of congeries of vessels was seen surrounding the apex of one renal papilla. This was removed and the hæmaturia ceased and the patient recovered. A slight relapse occurred eighteen months later.

The second patient was a woman, thirty years old, who had suffered from profuse hæmaturia for fourteen days without apparent cause. No renal cells, fragments of new-growth, tubercle bacilli, or tube casts were found in the urine. Cystoscopic examination showed the bladder to be healthy, but blood could be seen entering from the left ureter. Accordingly the kidney was exposed and together with the renal pelvis and the ureter it was found normal, but on opening the pelvis a bright red varicose papilla came into view. This was scooped out, the kidney closed and replaced, and there was no return of the hemorrhage.

Pousson[2] reports two cases illustrating the influence of distention of the kidney in the causation of hæmaturia. One occurred in a laundress, aged twenty-nine years, who suffered from pain in the loin, with hæmaturia. On examination the left kidney was found enlarged and painful. With the aid of the cystoscope blood was seen coming from the left ureter. The condition was thought to be dependent upon obstruction of the ureter by a calculus. The kidney was exposed, found to be enlarged, and uronephrotic. It was opened and much fluid escaped. A valve-like fold of the mucous membrane was found at the mouth of the ureter. This was divided and the wound closed, the kidney being sutured in place. The hæmaturia ceased, but infection of the wound resulted and the kidney was subsequently removed.

The second case occurred in a man, thirty-six years old, who had exhibited vague symptoms of renal colic at the age of twelve and hæmaturia at thirty. On examination the left kidney was found slightly enlarged and painful on pressure. With the aid of the cystoscope blood was observed escaping freely from the left ureter. Primary

[1] British Medical Journal, February 3, 1900, p. 248.
[2] L'Association Française d'Urologie, Paris, 1900, p. 100.

renal tuberculosis being suspected the corresponding kidney was exposed and found enlarged and fluctuating. On incision a round calculus extending into the ureter was disclosed. The renal tissue was stretched and thinned. Nephrectomy was performed.

J. Albarran[1] reports a case of hæmaturia attributed to unrecognized nephritis. The patient was a man, fifty-three years old, with pain in the right loin, radiating in the course of the ureter and attended with the presence of a small amount of albumin and at times red blood corpuscles in the urine. In conjunction with an exacerbation of pain copious hæmaturia occurred, and on cystoscopic examination blood was seen coming from the right ureter. A diagnosis of nephritis was made. On exposure of the kidney the organ was found enlarged, hyperæmic, and adherent, and when divided it appeared healthy except for the presence of a grayish nodule, the size of a millet-seed, at the base of a pyramid. This was enucleated and found to present the lesions of chronic nephritis. There was no return of the bleeding.

Loumeau[2] refers to a case of hæmaturia in a woman, thirty-four years old, in whom the blood came from the left kidney. The condition was thought to be due to primary tuberculosis, and as a last resort nephrectomy was performed. The hemorrhage ceased, but uræmic symptoms developed and death resulted in the course of fifteen days.

O. Pasteau[3] reports the case of a woman, forty-four years old, who complained of pain in the right lumbar region and presented signs of downward displacement of the kidney, later attended with hæmaturia. The kidney was exposed and sutured in its proper position. Mild attacks of pain, nevertheless, occurred, but there was no return of the hæmaturia.

Granville MacGowan[4] reports the case of a man, thirty-five years old, who, after lifting a heavy weight eight years previously, had an attack of profuse hæmaturia, which ceased spontaneously in the course of several days. Within two months the hæmaturia had returned and was becoming profuse. On cystoscopic examination the bladder was found normal, but blood could be seen coming from the right ureter. Suprapubic cystotomy was first performed, and later the right kidney was exposed and removed, although no lesion was found. The patient recovered and the condition was attributed to a general purpuric state.

F. Suter[5] reports the case of a woman, thirty-two years old, with an hereditary predisposition to tuberculosis, whose urine, passed without difficulty, had been turbid and bloody for a year and a half. On examination tenderness was elicited over the situation of the left kidney, without increased resistance or tumefaction. The urine contained blood corpuscles and squamous epithelial cells, but no renal elements and no tubercle bacilli. With the aid of the cystoscope the bladder was found to be normal, but bloody urine could be seen entering from the left ureter. Tumor or tuberculosis being suspected, lumbar nephrectomy was undertaken and successfully performed. The removed organ was found to be entirely normal, but the renal pelvis and the adjacent ureter were the seat of disseminated miliary telangiectasis.

[1] L'Association Française d'Urologie, Paris, 1900, p. 100.
[2] Ibid., p. 125.
[3] Ibid., p. 152.
[4] Medical News, December 7, 1901, p. 896.
[5] Centralblatt für die Krankheiten der Harn- und Sexual-Organe, 1902, Bd. xiii., Heft 1, p. 26.

A. T. Cabot[1] reports the case of a woman, forty-three years old, who had on several occasions had profuse hæmaturia, the only possible cause for which that could be found was downward displacement of the right kidney. Other measures failing to afford relief the suspected organ was exposed and restored to its proper position, and there was no further recurrence of the bleeding.

W. H. Jalland[2] relates the case of a man, thirty years old, who had for some time been suffering from pain over the right kidney, with frequent attacks of hæmaturia, and had also passed several small fragments of uric acid calculi. The pain increasing in severity, the right kidney was exposed and punctured in five or six places, but no stone could be detected. The organ was replaced, the wound healed, and there was no return of pain or of hæmaturia.

I have, for convenience of study, arranged the cases considered in this communication in tabular form. (See pages 652 and 653.)

An analysis of the 48 cases comprised in this tabulation yields the following results:

Sex. The sex is mentioned in 47—31 females, 16 males.

The condition thus appears to be more common in women than in men. The cause for this preponderance may, perhaps, be found to reside in the greater frequency of neurotic disorders in women, of displacements of the kidney, and of circulatory derangements due to constriction of the waist by clothing, or in disorders associated with pregnancy and lactation.

Age. The age of the patient is mentioned in 45 cases, the youngest being eighteen, the oldest seventy-six, the average thirty-six years. The distribution according to decades is as follows:

	Cases.
From 10 to 19 years	2
" 20 to 29 "	12
" 30 to 39 "	15
" 40 to 49 "	8
" 50 to 59 "	7
" 70 to 79 "	1

The great majority of cases—60 per cent.—are thus seen to come under observation during the most active period of life, that is, between the twentieth and the thirty-ninth year.

Kidney Affected. The bleeding came from the left kidney in 23 cases, and from the right kidney in 25 cases. This practical equality in the involvement of the two kidneys indicates that the disorder is not dependent upon local anatomical conditions.

Clinical Diagnosis. In almost all of the cases in which a diagnosis was recorded calculus or neoplasm or tuberculosis was suspected: in 1 nephritis, in 1 hæmophilia, in 1 hysteria, and in 1 angioma or angioneurosis.

[1] Boston Medical and Surgical Journal, March 6, 1902, p. 243.
[2] Lancet, May 3, 1902, p. 1280.

TABULATION OF CASES OF UNILATERAL RENAL HÆMATURIA.

Reporter.	Sex and age	Kidney affected	Clinical diagnosis.	Operation.	Morbid anatomy.	Result.	Pathological diagnosis.
Durham,	F. 43	Right	Calculus.	1. Kidney exposed; 2. Nephrectomy.	No abnormality.	Death.	
Lauenstein,	M. 47	Right	.....	Kidney exposed; pelvis opened; kidney punctured.	No abnormality.	Recovery.	
Anderson,	F. 24	Right	Calculus.	Kidney palpated, punctured.	No abnormality.	"	Neurosis.
Sabatier,	F. 30	Right	Calculous pyelitis.	Nephrotomy, nephrectomy	No abnormality.	"	Hæmaturic nephralgia.
Schede,	M. 50	Left	Calculous tuberculosis or malignant disease.	Nephrectomy	Kidney friable, anæmic, seat of petechiæ.	"	Local hæmophilia.
Senator,	F. 19	Right	Hæmophilia.	Nephrectomy	Nephritis.	"	Renal hæmophilia.
Abbe,	...	Right	.....	Decapsulation, puncture.	Gritty point at papilla of pyramid.	"	
Legueu,	M. 26	Left	.....	Decapsulation.	Kidney displaced and movable.	Death.	Idiopathic renal neuralgia.
Stavely,	F. 39	Left	.....	Nephrotomy.	No abnormality.	Recovery.	
Stavely,	F.	Left	Neoplasm.	Nephrotomy.	Nephritis.	"	
Israel,	F. 42	Left	Neoplasm.	Nephrotomy.	No abnormality.	"	
Broca,	F. 28	Right	Tuberculosis or neoplasm.	Decapsulation, palpation.	No abnormality.	"	
Picque and Reblaub,	F. 76	Left	Malignant disease.	Decapsulation, evacuation of cyst, excision of cyst wall, nephrotomy.	Cyst of kidney.	"	
Picque and Reblaub,	F. 39	Right	Neoplasm.	Kidney exposed.	No abnormality.	"	Vasomotor disorder.
Oliver,	M.	Left	.....	Kidney probed, nephrotomy.	No abnormality.	Death.	Nephritis.
Oliver,	M. 54	Right	.....	Kidney exposed.	Kidney shrivelled.	Recovery.	
Elb,	M. 22	Left	Morphinism.	Nephrectomy	No abnormality.	"	Angioneurotic hæmaturia.
Guyon,	M. 26	Right	Tuberculosis.	Nephrotomy.	No abnormality.	"	
Guyon,	F. 35	Right	Carcinoma.	Kidney exposed.	No abnormality.	"	Congestion; lactation.
De Keersmaecker,	F. 43	Left	.....	Nephrectomy	Chronic nephritis.	"	
Debaisieux,	F. 20	Left	Neoplasm or calculus.	Nephrotomy.	Minute translucent prominences in pelvis of kidney.	"	
Dandois,	F. 30	Right	.....	Nephrotomy.	Congestion.	"	Pregnancy.
Harris,	M. 50	Left	Angioma or angioneurotic hæmaturia.	Nephrotomy.	No abnormality.	"	
Genouville,	M. 51	Right	Calculus or neoplasm.	1. Decapsulation, nephrotomy; 2. Nephrectomy.	False membrane in pelvis of kidney.	"	Secondary hydronephrosis.
Genouville,	M. 35	Right	.....	Nephrotomy.	Kidney large, hyperæmic; capsular adhesions.	Recurrence.	

Reporter.	Sex and age	Kidney affected	Clinical diagnosis.	Operation.	Morbid anatomy.	Result.	Pathological diagnosis.
Demons,	F. 24	Left	.....	Nephrectomy	Sclerosis of kidney.	Recovery.	
Loumeau,	F. 32	Left	.....	Nephrotomy.	Congestion.	"	
Debersaques,	M. 38	Left	.....	Nephrotomy; sound introduced into ureter.	Congestion.	"	
Poirier,	F. 43	Right	Calculus.	Nephrectomy	Chronic nephritis.	Death.	
Pousson,	F. 28	Right	Primary renal tuberculosis or epithelioma.	Nephrotomy; nephrectomy.	Chronic nephritis.	Recovery.	
Potherat,	F. 52	Right	Neoplasm.	Nephrectomy	Chronic nephritis.	Death.	
Rovsing,	F. 21	Right	.....	Nephrotomy.	Kidney adherent, cyanotic, necrotic, thrombotic.	Recovery.	Compression by liver.
Rovsing,	F. 56	Right	.....	Nephrotomy.	Kidney displac'd, cyanotic.	"	Tight lacing.
Rovsing,	M. 47	Left	Neoplasm, or tuberculosis.	Nephrotomy.	Kidney displac'd.	"	Possibly small unobserved tuberculous focus or other lesion.
Rovsing,	F. 28	Left	Calculus.	Nephrotomy.	Kidney displac'd, pelvis dilated, ureter bent, bacteria in straight tubules	"	Kidney movable.
Myles,	F. 36	Left	.....	1. Pelvotomy, bougie introduced into ureter, puncture of kidney, nephropexy. 2. Nephrectomy.	1. Kidney movable, enlarged, congested, lobulated. 2. Myxangiomatous change in renal pelvis.	"	
Fenwick,	F. 18	Left	Hysteria or calculus.	Pelvotomy, telangiectasis removed.	Papillary telangiectasis.	Recurrence.	
Fenwick,	F. 30	Left	.....	Pelvotomy, telangiectasis removed.	Papillary telangiectasis.	Recovery.	
Pousson,	F. 29	Left	Calculus.	1. Pelvotomy. 2. Nephrectomy.	Kidney enlarged, uronephrotic, valve-like fold in pelvis.	"	Distention of kidney.
Pousson,	M. 36	Left	Primary renal tuberculosis.	Nephrectomy	Kidney enlarged, fluctuating calculus; renal tissue stretched.	"	Distention of kidney.
Albarran,	M. 53	Right	Nephritis.	Nephrotomy.	Kidney enlarged, hyperæmic, adherent; grayish nodule at base of pyramid.	"	Chronic nephritis.
Loumeau,	F. 34	Left	Primary renal tuberculosis.	Nephrectomy	.....	Death.	Uræmia.
Pasteau,	F. 44	Right	Nephropexy.	Nephropexy.	Kidney displac'd.	Recovery.	
MacGowan,	M. 35	Right	.....	Nephrectomy	No abnormality.	"	General purpuric state.
Suter,	F. 32	Left	Neoplasm or tuberculosis.	Nephrectomy	Disseminated miliary telangiectasis of renal pelvis.	"	
Cabot,	F. 43	Right	.....	Nephropexy.	Kidney displac'd.	"	
Jalland,	M. 30	Right	.....	Puncture.	No abnormality.	"	
Eshner,	F. 20	Right	Calculus.	Kidney exposed.	No abnormality.	"	

The diagnosis is exceedingly difficult and can be made only by excluding other causes of hæmaturia. That the bleeding comes from one kidney alone can be demonstrated by cystoscopic examination or ureteral catheterization or direct inspection of the vesical orifices of the ureters after cystotomy.

OPERATIVE PROCEDURE. The operation consisted in—

	Cases.
Simple exposure of the kidney, probably with palpation in	4
Exposure of the kidney, with puncture in	2
" " " with pelvotomy and puncture in	1
Nephropexy in	2
Decapsulation of the kidney in	2
" " " with puncture in	1
Nephrotomy in	14
Pelvotomy, with removal of telangiectases, in	2
Decapsulation of the kidney, with removal of a cyst, removal of the cyst wall, and nephrotomy, in	1
Nephrotomy, with probing, in	2
Nephrectomy in	10
Exposure of the kidney at a primary operation, followed by nephrectomy at a secondary operation, in	1
Nephrotomy and nephrectomy in	2
Decapsulation of the kidney, with nephrotomy at a primary operation, followed by nephrectomy at a secondary operation, in	1
Pelvotomy, with probing and puncture of the kidney and nephropexy at a primary operation, followed by nephrectomy at a secondary operation, in	1
Pelvotomy at a primary operation, followed by nephrectomy at a secondary operation, in	1

The preferable course of procedure would seem, after medicinal and other non-operative measures have failed to check the hemorrhage, to consist in exposure of the kidney, with incision of the organ itself or its pelvis or stripping of its capsule, and the removal of any local lesion, or the restoration of a displaced organ. Should the hæmaturia, nevertheless, persist, nephrectomy may be resorted to as a final expedient.

RESULT. Recovery ensued in 40 cases, death in 6, and recurrence in 2. Of course, it is possible that in some of the cases disease latent at the time of operation may have become manifest at a later date, and in others the cessation of the hæmaturia may not have been permanent. Nevertheless, the prognosis must be considered favorable with appropriate treatment.

MORBID ANATOMY. In 16 of the cases no lesion was discovered at operation, or at least was recorded, but failure in this direction does not necessarily imply absence of lesions, as in almost all of these, if not all, histological examination of tissue from the affected organ was not undertaken. Displacement or undue mobility of the kidney was present in 6 cases, renal congestion in 3, adhesions of the kidney in 2, inflammatory, degenerative, or other destructive lesions of the kidney in 11, alterations in the pelvis of the kidney in 9. It will be noted

that it is particularly in the earlier cases that the kidney is recorded as being healthy, while in almost all of the later cases structural changes are noted.

Various explanations have been suggested for the hæmaturia in the cases under consideration, as well as for the cessation of the phenomenon after simple exposure or manipulation or incision of the kidney. No doubt the cause is not the same in every case, as the evidence goes to show. In by far the larger number of cases in which histological examination has been undertaken lesions of an inflammatory character have been found. In some vascular changes or capsular adhesions have been noted. In a considerable number there has been mobility or displacement of the kidney sufficient to give rise to circulatory disturbances. In some, perhaps, lesions were present, though not appreciable to the naked eye. Only exceptionally could the kidney be considered healthy after histological examination. It is probable that none of the cases was an example of true hæmophilia. The suggestion of a vasomotor or angioneurotic condition does not seem an adequate explanation, and for the present it must be confessed that in a certain number of cases the cause of the hæmaturia, as well as its localization to one kidney, remains obscure. We are equally in the dark as to the mechanism through which the bleeding is controlled in the sequence of mere exposure, manipulation, or even incision of the kidney. Perhaps we have here an analogy with the recovery that sometimes follows abdominal section in cases of tuberculous peritonitis. It has also been shown that the symptoms of nephritis may be relieved by division or stripping of the caspule of the kidney, or puncture of the organ, probably through circulatory modifications thus brought about. A similar explanation may be applicable to the results of appropriate operation in the presence of adhesions or displacement, or mobility of the kidney.

That the kidney may be the seat of disease when thought to be healthy is shown by the demonstration made by Nicolich[1] before the meeting of the French Urological Society, October 24, 1901, of a kidney from a patient operated upon with success for the relief of hæmaturia designated essential and reported free from lesion, but which, on further examination, was found to present histological appearances of glomerulo-nephritis.

A case that is interesting, among other things, from the therapeutic standpoint has been reported by J. Passet.[2] The patient was a married woman, in whom hæmaturia set in at the menstrual period and persisted beyond. The condition was thought to be due to detachment of a papilloma of the bladder. The urine was, on examination,

[1] Annales des Maladies des Organes Genito-Urinaires, 1901, p. 1376.

[2] Centralblatt für die Krankheiten der Harn- und Sexual-Organe, 1894, v. p. 397.

found to contain only red and white blood corpuscles. The bleeding ceased after the injection of a solution of silver nitrate, but it recurred after an interval of nineteen months, following some emotional disturbance. The hæmaturia now failed to yield to treatment, and the patient declined to submit to operation. Digital examination disclosed the presence of a coarsely granular and trabeculated area on the posterior wall of the bladder. The condition of the patient became so grave that operation was insisted on. Accordingly suprapubic cystotomy was performed, but no lesion of the bladder was disclosed. On introducing a catheter into each ureter blood was seen to escape from the right. The hæmaturia ceased on the following day, without further manipulation. It returned, however, after the lapse of twenty-one months, but it ceased with rest in bed, and it had not returned eleven months later. The condition is believed to have been one of local hæmophilia.

A somewhat analogous case has been reported by Potherat.[1] The patient was a woman, thirty-three years old, who had suffered from profuse hæmaturia for four years, and presented an anæmic appearance. On examination it was thought that the kidneys were not increased in size, but rather smaller than normal. There was, however, slight pain in the right costo-vertebral angle on manipulation. On cystoscopic examination and ureteral catheterization blood was seen escaping from the right ureter. The urine contained albumin in considerable amount. Subsequent attempts at ureteral catheterization for the study of the urine from each kidney proved unsuccessful, but the hæmaturia ceased and did not recur.

In neither of these cases, it will be noted, was the suspected kidney exposed, so that no definite opinion can be formed as to whether it was diseased or not. The cases, though instances of unilateral renal hæmaturia, are, therefore, not included in the foregoing tabulation.

The following case can scarcely be considered one of unilateral renal hæmaturia, inasmuch as the hemorrhage failed to cease after the removal of the kidney suspected to be the source of the bleeding. Of course, the other kidney may have been the one at fault, but of this there is no evidence.

At a meeting of the Société de Chirurgie held June 8, 1898, Nimier[2] reported the case of a young man, seventeen years old, who suffered from hæmaturia, with remissions, for four years following an injury to the left side of the abdomen.

There had been colicky pain in the course of the left ureter, with tenderness on palpation. The urine contained numerous red blood

[1] Bulletin et Mémoires de la Société de Chirurgie de Paris, 1898, p. 634.

[2] Ibid., 1898, xxiv. p. 631; also Annales des Maladies des Organes Genito-Urinaires, 1898, p. 281.

corpuscles, a small number of leucocytes, but no bacteria or other parasites. Nothing abnormal being found on cystoscopic examination, the left kidney was exposed and found indurated at its superior pole. The organ was incised and on section presented a grayish-yellow appearance. A neoplasm being suspected the kidney was removed, but the hæmaturia persisted. On histological examination a slight degree of sclerosis of the kidney was found at one point only, with proliferation of embryonal cells.

Conclusions. There occurs occasionally, in men and women alike, mostly at middle adult life, hemorrhage from a single kidney—from either with equal frequency, in many instances in consequence of demonstrable organic disorder, and in the remainder of obscure and undetermined origin. This hæmaturia may cease after simple exposure of the kidney, or after nephropexy or nephrotomy, or in the failure of these after nephrectomy.

Note.—Since the foregoing communication was read I have come across the report of an additional case in which slight mobility of the kidney was attended with profuse hæmaturia.[1] A middle-aged woman presented herself on account of pain in the right loin, frequency of micturition, and hæmaturia. Five years previously she had been seized with pain in the right loin, associated with the presence of a small amount of blood in the urine. Her medical attendant suspected the presence of a calculus, but no conclusive evidence was discoverable. Attacks of pain recurred, and hæmaturia took place from time to time. There had been loss of weight and strength. Tenderness was present in the right loin, and the right kidney seemed larger than the left, and it moved more with respiration. The bladder was examined under anæsthesia, and was found healthy. The urine contained blood and pus cells, but no crystals, or casts, or tubercle bacilli. The right kidney was exposed, and found enlarged and congested. It was incised and explored, but no stone or obstruction or other abnormality was found. The organ was sutured in place. Recovery was uninterrupted, and there was no recurrence.

In another case hæmaturia of four years' standing was associated with chronic parenchymatous nephritis, and ceased after operation on the kidney.[2] The patient was a farmer, forty years old, who for four years had not noticed the urine to be dark in color, and an examination disclosed the presence of blood. The condition was thought to be dependent on the presence of a stone in the bladder. There was increased frequency of micturition, and the appearance was anæmic, but there had never been a chill or febrile attack, and there was no elevation of temperature

[1] R. Earle Newton. Australasian Medical Gazette, December 23, 1902, p. 622.
[2] C. H. Chetwood. Medical News, February 7, 1903, p. 256.

and no evidence of pulmonary or cardiac lesion. The urine was uniformly bloody. It contained red blood corpuscles, but no pus, no tube casts, and no tubercle bacilli. On palpation a slight amount of tenderness seemed present over the lower pole of the right kidney. The prostate gland was not enlarged, no stone could be detected in the bladder, and no lesion of the urethra discovered. On cystoscopic examination blood was seen issuing from the right ureter, while the urine from the left ureter was clear. The right kidney was, accordingly, exposed and divided, but the only abnormality found was a small indurated area on the anterior surface near the pelvis. This was incised and a small piece removed for microscopic examination. The blood disappeared from the urine in the course of three or four days, and it did not thereafter reappear. Histological study of the tissue removed disclosed the lesions of chronic parenchymatous nephritis.

BENCE JONES ALBUMOSURIA, WITH PECULIAR NERVOUS PHENOMENA.

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The attention that has been devoted to this subject during the past decade appears to warrant the recording of such cases; and while these reports have been more or less isolated—nine occurring in America—and have appeared under a variety of titles, as osteomalacia, osteosarcoma, carcinoma of the bones, lymphatic leukæmia, pernicious anæmia, myxœdema, etc., the majority, and possibly all, have been associated with new-growths of the bony skeleton, which should probably be regarded as multiple myeloma. In three examples, with a review of the literature, reported in collaboration with Dr. J. M. Anders,[1] deformities of both the long and flat bones were detected ante-mortem in one of them; in another there was considerable recent deformity at the site of the fracture of the ankle.

The patient who forms the basis for this report first came under my care two years ago, at which time she was found to be suffering from gastro-intestinal catarrh.

Mrs. L., widow, aged fifty years, housewife, and of American birth. Her family history gave nothing of interest. Had the diseases of childhood; two children, both now living, the younger a daughter, aged twenty years. There had been a tumor developing in the left breast during the past eight years, and in 1898 this breast was removed by Dr. T. S. K. Morton, who stated that the growth was a carcinoma, but up to the present time there is no perceptible return of the trouble.

There have been repeated attacks of obstinate constipation, lasting from one to five days, at which times the abdomen became hard and nodular, and there were intense abdominal pains, accompanied by paroxysmal vomiting. Vomiting without apparent cause has been a prominent feature, while both lancinating, dull, and boring pains arising in the back and pelvis and radiating to the umbilicus and pubes have comprised the most distressing symptoms during the past six months. There has often been a feeling of "giving away" of the left leg and the bones of the left pelvis while walking or when ascending the stairs. These pains were agonizing, compelling her to cling to the nearest object for support.

Within the last five years her weight has been reduced from 185 pounds to 95 pounds; the greater portion of this loss has taken place during the past year, however. Together with the rapid loss of flesh and strength there developed œdema beneath the eyes, pallor of the skin and mucous surfaces, frequent attacks of urticaria, and cutaneous abscesses of the scalp and dorsal surface of the chest.

Early in January, 1902, she received a fall, inflicting a lacerated wound of the occiput and rather severe contusion of the left shoulder. It was not until six weeks later that the peculiar urinary phenomenon (albumosuria) was detected.

Neuralgic pains in the left shoulder which radiated to the left hand were most annoying, and often prevented sleep. There were, at times, numbness and a feeling of "pins and needles" in the left arm and hand. The left thigh, leg, and foot have also been painful, and at night these pains became cramp-like, causing muscular contraction. The great and adjacent toes of the left foot were anæsthetic to deep prick of a pin, and sensation was impaired over the inner surface of the foot and leg. Over these regions there was inability to distinguish between hot and cold. There was no apparent atrophy of either the foot or leg, and the muscles reacted normally. The left knee-jerk and the plantar reflex were decidedly increased, and ankle clonus was marked. Other reflexes normal.

The heart's action was regular at 70 beats per minute; no murmurs were audible, but there appeared to be a lack of muscular element with the first sound. The radial and temporal arteries were atheromatous. Lungs and the abdominal viscera normal.

There had been failing of vision during the past year, and I am privileged through the courtesy of Dr. L. Webster Fox to add his report of an ophthalmoscopic study: "The right eye shows slight diffused retinitis, with possibly posterior vitreous changes, which are so slight, however, that I cannot differentiate between the posterior part of the vitreous and that of the retina. I am inclined to believe this haziness to be retinitis. There is marked sclerosis of the blood-vessels, the arteries more pronounced than the veins. There does not seem to be the normal difference between the arteries and veins. The optic nerve is hazy, although I can find no deposits of albuminoids in the retina, and there are no hemorrhages. The left eye shows the same appearance as the right. The pupils respond to light sluggishly. The lessened vision is due to interference with the media."

The urine was first noted to give the reaction for the Bence Jones body March 12, 1902. Repeated examinations were made during the

following month, all of which showed this substance to be present. More recently, however, the results of a number of examinations have been negative; while those of others where the urine was collected during the same week have given positive reactions, which places this case in the category of those reported by Kahler,[2] and by Kuhne and Stokvis,[3] where the albumosuria was intermittent. The urine was acid in reaction, specific gravity 1008 to 1012, light amber or water color, often turbid, and the twenty-four hours' product equalled 1200 c.c. A trace of serum albumin was always present. Microscopically, the sediment contained epithelial cells, amorphous urates, and a few leucocytes. No renal casts were seen.

The methods employed for the study of Bence Jones albumose were those suggested by Henry Bence Jones,[4] Huppart,[5] Matthes,[6] Milroy,[7] paper and Magnus-Levy,[8] and have been considered in a previous paper upon this subject;[1] and Dr. Simon has thoroughly considered these reactions in a contribution to this JOURNAL for May, 1902.

During the past year there has been decided pallor, though many of the general symptoms commonly known to accompany such blood impoverishment were wanting. An examination of the blood July 14, 1902, gave: Red cells, 4,430,000 per c.mm.; white cells, 8600; hæmoglobin, 39 per cent. The differential leucocyte count showed: Polymorphonuclear cells, 39 per cent.; large mononuclear, 15.25; large lymphocytes, 20; small lymphocytes, 21.5; eosinophiles, 2.25; transitionals, 2. Other examinations gave results which differed but slightly from the above except in the quantity of hæmoglobin, which reached 55 per cent. on one occasion. The erythrocytes were always found to be above 4,000,000 and the leucocytes below 8600. Here the anæmia appears to be of a chlorotic character, the hæmoglobin alone suffering loss. Stained specimens displayed a high grade of poikilocytosis, and microcytes and macrocytes were occasional findings. No nucleated red cells were detected. The pronounced increase in the mononuclear leucocytes to 56.75 per cent., with a reduction of the polymorphonuclear elements to 39 per cent., appears worthy of special mention.

Albumosuria developed after the removal of a rodent cancer from the nose, in the case reported by Bradshaw and Warrington.[9] It appears difficult to show, in my case, that the albumosuria has any relation whatever to the cancerous growth removed from the breast four years previously.

Senator,[10] in 1897, called attention to certain nervous phenomena appearing with albumosuria. His patient, a female, aged thirty-six years, suffered from paralysis of the hypoglossal nerves, paresis of the arytenoideus, and anæsthesia throughout the course of distribution of the trigeminal nerve.

Fitz[11] observed the case of a female, aged forty-nine years, who complained of a sense of numbness in the right heel, knee, and fingers of the right hand. The teeth were painful, and changes in the voice, tongue, skin, and its appendages were also present. Fitz regards this case as one of myxœdema with albumosuria.

James H. Wright[12] has reported the case of a male, aged fifty-four years, in whom there were numbness of the feet, double vision, and strabismus. The knee-jerks were exaggerated and ankle clonus pronounced.

L. P. Hamburger,[13] in the first case reported by himself, refers to repeated attacks of facial neuralgia. The patient was a female, aged forty-nine years.

A. Raschkes'[14] case was that of a female, aged forty years. The initial symptom was momentary, cramp-like pains in the right foot.

Case I. of the series reported with Dr. Anders suffered continuously from cranial and facial neuralgia. Case II. often referred to a tingling sensation of both the hands and feet and of neuralgic pains in the lower limbs; while in Case III. there was paralysis of the left side of the face. In reviewing the records of cases furnished by the literature, cephalalgia and neuralgia are among the most constant of symptoms, yet in the case herein reported cerebral pains have been infrequent.

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ON A NEW METHOD FOR THE APPLICATION OF WIDAL'S TEST FOR THE DIAGNOSIS OF TYPHOID FEVER.

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Of the many technical applications of the Widal reaction, the most popular as well as the most practical is the dried-blood method of the

late Dr. Wyatt Johnson; and the extension of his method which I am about to describe will, it seems to me, tend to add to its utility as well as to its accuracy. The technique is very simple. A loop from the feces of the suspected case is smeared upon the surface of an agar slant in a prepared tube and sent to the laboratory just as diphtheria cultures are prepared. In the absence of an agar tube a small piece of paper soiled with the feces may be sent in a tightly closed bottle. From this first specimen one or more bouillon cultures are prepared. The bouillon must react from 1 to 2 per cent. *alkaline* with the $\frac{N}{10}$ acid, using phenolphthalein as the indicator. The infected bouillon is now incubated at the usual temperature for twelve hours, when we are ready to make the examination. A sample of the blood is taken at the same time the specimen of the feces is procured. This is mixed with the bouillon culture by the usual procedure and placed upon the stage of the microscope. If now there is sufficient agglutinative material present the typhoid bacilli (if they exist in the culture) will very shortly form clumps in the fields, which will be observed full of colon bacilli in active motion; and if this reaction does occur we can, of course, safely say that the case has advanced at least to the second week of the disease. Should no reaction take place, another sample of the bouillon culture is tested with the blood from an advanced case of typhoid fever, the agglutinative power of which has been tested by the ordinary method, with a pure culture of the bacillus of Eberth. Indeed, it is necessary for the proper use of this test to keep in stock a number of specimens of blood from well-marked typhoid cases. These can be kept in a dry place, and they retain their power to produce a reaction with a pure culture, probably indefinitely. With this blood, if the feces contain any typhoid bacilli, a positive and distinct reaction will shortly occur, the clumps of typhoid bacilli being more or less numerous according to the number of typhoid organisms present, while the still motile colon bacilli occupy the rest of the field, and are seen to be in active motion. This indicates that the case is one of typhoid fever, and that the disease is in the early stage, at least from the middle to the end of the first week. By means of this simple method we are enabled, in my opinion, to make an accurate diagnosis in the early stages of the disease when the other symptoms may be more or less masked, and thus remove many elements of doubt in a suspicious case.

On the other hand, we are enabled to state that the patient has advanced at least into the second week of the disease, or beyond the seventh day if his own blood produces a positive reaction by my method. One might easily conceive, of course, that rare condition of a second attack within a period too brief to destroy the agglutinative reaction of the blood, the result of the *first* attack of the disease; but such an exception must be extremely rare, and would produce much

more chance for error by the ordinary application of the Widal test. I am well acquainted with the fact that certain observers claim that they have been unable to discover the presence of the typhoid bacillus in the feces previous to the eleventh day of the disease; but from the distinct reactions which I have obtained by my method (which, almost without exception, in the cases in which I have used it has produced clumping in the very early stages of the disease), and which, by this method alone, I have been enabled to diagnose typhoid fever I am certain that the bacillus of the disease *is* present in the feces quite a time before the outbreak of the symptoms.

In thirty-five tests which I have made within the past six months of cases in the earlier stages of the disease, every case that gave a positive reaction by this method turned out to be typhoid fever, while in a large number of other tests from which *no* reaction was obtained I do not know of one in which this method has given even a *doubtful* reaction.

If it is true that the agglutinative material in typhoid blood reacts by producing clumping with the typhoid bacillus, and does not give a reaction with the colon bacillus, then there is no reason why this method should not prove of great utility in the bacteriological laboratory as well as to the general profession.

I have avoided, in this short notice, commenting upon the many sources of error which have in no small degree tended to affect the accuracy as well as the utility of the Widal test. While I am conscious of the fact that my extension of the Widal method has only been tested upon a limited number of cases, still it has been productive of such good results, and is so full of possibility that I have felt it incumbent upon me to place it before the profession.

LATE SYSTOLIC MITRAL MURMURS.

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In The American Journal of the Medical Sciences for September, 1892, Griffith reported three cases in which the murmur of mitral regurgitation was heard after the apex beat and the first sound of the heart, instead of synchronously with and following them. In the *Medical News* for October 20, 1894, I reported a similar case, but with a different explanation. Since that time I have heard many such late murmurs of mitral insufficiency, and Griffith has told me that he encounters them frequently. Other physicians have occasionally reported their occurrence, but no generally accepted explanation of the late development of the murmur has been advanced.

I will here briefly report a typical case, as a basis for a closer study of the peculiarity of the murmur.

Mrs. A. N., aged thirty-five years, German, in Colorado four years; family history negative. She has suffered an attack of acute rheumatism, but has been well otherwise since childhood. Her four labors have been uneventful. She complained of rheumatic pains in the wrists, of slight swelling of the feet and the lower eyelids, of dyspnœa upon exertion, with occasional nose-bleed.

Her pulse was regular, 60 per minute, of good tension. Temperature normal. Tongue slightly coated. Feet and eyelids slightly œdematous. Examination otherwise negative, excepting as regards the heart. By percussion this organ was enlarged to just beyond the nipple line at the left, and slightly to the right. The apex beat was just outside the line mentioned, in the left space. In the mitral area was heard a murmur transmitted three inches to the left, and slightly in other directions, but most distinct just under the nipple, beginning abruptly after the occurrence of the apex beat and first cardiac sound, and ceasing just before the second sound. No other murmurs. No reduplication nor accentuation of the basic sounds. No anæmic hum in the neck, or other signs of anæmia. The murmur was of the blowing character commonly found in this location.

The urine was acid in reaction, high in color, specific gravity 1029, no albumin or sugar.

Dr. Henry Sewall kindly saw her with me, and we found the condition as at first examination. With the differential stethoscope, one bell applied over the place of the murmur, and the other over the lower end of the sternum, we were able to note very easily the difference in time between the apex beat and the beginning of the murmur. Dr. Sewall, who has done much original work with the instrument in question, both in clinical and in physiological study of the heart's action, stated that he could distinguish a cardiac contraction synchronous with the beginning of a murmur, and, of course, later than the apex beat. At the meeting of the Colorado State Medical Society in June, 1896, the case was exhibited, and many physicians examined the heart. Apparently owing to the excitement its action was peculiarly forcible, and hence the characteristics of the murmur were very distinctly shown. Drs. Dennison, Whitney, Hershey, Packard, and many others examined the case, under favorable circumstances, and there was no discrepancy as to the facts, viz., that the area of cardiac dulness and the time of the murmur were as stated, and that the latter was transmitted to the left. There was much discussion as to the manner of origin of the murmur. All agreed that the mitral valve was incompetent.

Griffith's explanation of the peculiar time of this murmur is, that it is the ordinary sound of mitral leakage, with the exception that in its earlier stages the regurgitant current gives rise to no vibrations perceptible to the human ear as sound. I see no reason why this explanation may not apply in certain cases. After considerable study, however, I am satisfied that the explanation offered with my first reported case more nearly meets all the difficulties we encounter, in these cases,

than any other. That explanation was as follows, viz., that the first cardiac sound and the apex beat were due to the contraction of the right ventricle and closure of the tricuspid valve, the latter being presumably free from disease; and that the murmur was caused by regurgitation through a diseased mitral valve, and was later in time than the apex beat because of a tardy contraction of the left ventricle. In other words, if the mitral valve had been normal, so that no leakage could have occurred, we should have had a case of reduplication of the first sound, other conditions remaining the same.

If this particular case is to be explained upon the theory of Griffith, the murmur should have begun gradually, resembling, in its mode of beginning, the presystolic murmur of mitral stenosis. In my opinion a murmur beginning with a sharp puff must depend upon some sudden change in the hydraulic conditions within the heart, not upon a continuous regurgitant current, giving rise at a certain point to audible vibrations, which instantly reach their fullest intensity, all of which conditions would be necessary for a satisfactory explanation according to the theory mentioned. I conceive that a sharply beginning murmur must take origin in a sudden contraction of the walls of the cavity of the heart involved, or in a sudden yielding of the valve from inability to withstand the pressure of the contained blood. We should mention, however, that in none of the cases heretofore recorded has this sharp beginning of the murmur been especially noted, although I have recognized it probably a dozen times since.

It has long been known that reduplication of the basic sounds of the heart is frequent in mitral disease, and certain French authorities lay great stress upon this phenomenon in the diagnosis, especially of mitral stenosis. Most clinicians, I believe, recognize this reduplication, and accept the usual physiological explanation, viz., that it depends upon asynchronous contraction of the two ventricles. The right ventricle, owing to the increased tension in the pulmonic arterial system, dependent upon the mitral disease, anticipates the left by an instant. Thus we find in these very cases of mitral insufficiency we should *a priori* expect such asynchronism.

In a proportion of these cases we should also expect to find basic reduplication as a complement to the asynchronous ventricular contraction, since contractions beginning at different times might be expected to end likewise. Dr. Sewall has called attention to the fact that all grades of variation from the normal of the basic sound of the heart, from a simple indistinctness in the single sound, to distinct doubling may be detected. Since my attention was drawn to this point by him I have frequently noted the presence of a splitting of the second sound in the cases of late mitral murmur. It was easily recognized by both of us in one instance which I saw with Sewall a few years ago.

We have implied above that such a murmur might arise from the yielding of a valve after it had successfully withstood the pressure of the first part of the systole. We may conceive that disease of the papillary muscle supporting a segment of the mitral valve might so weaken it that it should be unable to stand the prolonged strain of the systole, although able to close the orifice by its contraction for an instant. Because of the brief duration of the maximum intraventricular pressure, however, this condition could not probably explain very late systolic murmurs, for if the valve did not yield during the time of highest pressure it would be unlikely to do so later. I do not, however, believe that this explanation applies to the case in hand.

Roy and Adami have shown that the final act in ventricular contraction is a pulling in of the auriculo-ventricular curtains by contraction of the papillary muscles. This causes a perceptible increase in the intra-ventricular pressure. If we may conceive that this pressure, in a given case, before their contraction, was so great that the action of the muscles, perhaps weakened by disease, was delayed an instant, and that, with the contraction, owing to dilatation of the ventricle and consequent spread of the base of support, the valve curtains were pulled apart, permitting regurgitation, we should have a beautiful theory of the origin of the late mitral systolic murmur.

I conclude, then, that in general we may explain these murmurs by asynchronous ventricular contraction. This theory is supported by the recognized frequency of such abnormal action of the heart in those cases in which the pressure in either system is abnormally increased. The right ventricle anticipates the contraction of the left in mitral disease, as we have seen, while the converse probably occurs in interstitial nephritis and other diseases raising the systemic tension above the normal. Confirming this hypothesis we have the recognition of basic reduplication in certain of the cases studied. I admit the plausibility in some circumstances of Griffith's explanation, and the possibility of the above-mentioned anomalous action of the papillary muscles in others.

CONCERNING THE ROLE OF INTRACELLULAR CATALYTIC PROCESSES IN THE PATHOGENESIS OF MALIGNANT NEOPLASMS.

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It is now accepted as one of the truths of physiology, as well as pathology, that the cells of the mammalian organism may change their form, and even at times their structure, during their existence. Physi-

ologically, they may change their forms under the influence of age, and according to many extrinsic and intrinsic influences to which they are subjected. It is often impossible to draw sharp lines of demarcation between that which is normal and that which is abnormal in such changes. Virchow expressed himself in the words that in reality there is no distinct line of demarcation between "physiological and pathological processes, and that the latter are only physiological processes which take place under difficult conditions." Cancer pathogenesis may accordingly be looked upon, in part at least, as a problem of growth of cells under difficult conditions, and in that case we have a right to expect that the solution of this problem may be aided by the adaptation and application of recent discoveries in physical chemistry to the pathology of cell growth, just as physical chemistry by its revelations concerning osmosis and the ionic theory has thrown light upon normal cell growth.

We have learned to look upon the individual cell as representing in itself a highly complicated system of organized parts, the latter standing in most intimate co-relation with each other. The cell may be conceived as representing on a small scale that which the entire cell state is on a grand scale, *i. e.*, a unity, a specific system of organized parts. Shall we seek the cause of malignant neoplasms, conditions of cell anarchy, caricatures of normal developmental processes, within or without the cell? This question separates all hypotheses concerning the etiology of malignant neoplasms into two great groups:

First, those assigning the cause of cancer to qualities inherent in the cells themselves. Secondly, those assigning the etiology of cancer to the action of some extraneous poison, particularly to the influence of micro-organisms. Although the latter theory may logically include the effect of toxins, even those not of bacterial origin, these two great groups may be concisely designated as, first, the histogenetic, and second, the parasitic theory, on the origin of cancer.

It is not my intention to discuss in this report the relative merits and demerits of these two groups of hypotheses. These matters are set forth in the various works on pathology, but most forcibly, perhaps, in the work of Professor David von Hansemann, *Die Mikroskopische Diagnose der Bosartigen Geschwülste.* Also in the work by Lubarsch, *Zur Lehre von den Geschwülsten*, in Ribbert's work, *Lehrbuch der allgemeinen Pathologie*, and in various editions of Lubarsch and Ostertag's *Ergebuisse d. Pathologie.* Hansemann, Ribbert, and Lubarsch are opposed to the parasitic theory, and by far the greater number of prominent German pathologists, while they are non-committal, have not given support to it. Recent American research work by R. B. Greenough, and Edward H. Nichols, published under the auspices of the Harvard University Cancer Commission, in the *Journal of Medical*

Research, 1902, vol. ii., invalidate the parasitic theory. On the other hand, the histogenetic theories, as examples of which we may mention those of Thiersch, "Der epithelial Krebs," Leipzig, 1865; Cohnheim, (*Allgemeine Pathologie*, Bd. i., S. 723) and Ribbert (l. c.) have the advantage that they cannot be controverted at all, being hypotheses pure and simple, without experimental foundation, so that they cannot be tested experimentally. The only excuse for the formulation of an hypothesis is that it gives the incentive to experimental investigation, and the formulation of inquiries into the nature of the thing discussed; and an hypothesis that does not permit of this has thrown no light on the subject to be solved, but simply side-tracked it. Thiersch conceived that the connective tissue might become weakened by disease or old age, and thereafter the epithelial tissues gain the supremacy and penetrate into the depths of other tissues. This theory does not explain the occurrence of cancer in young people, and cannot be tested experimentally.

Cohnheim conceived the cause of malignant neoplasms to be the supposed existence of congenital embryonal cells, which have remained latent in different tissues of the body. This theory does not explain why such undifferentiated embryonal cells, if they really occur, should suddenly begin to proliferate in an unrestricted manner.

This theory of Cohnheim has not become more probable by the discovery of unutilized segmentation cells of the frog by Roux,[1] who observed that in this animal, cells occurred which were not utilized, and were surrounded by growths of other cells. Barfurth observed the disruption and subsequent continued growth of a segmented portion of the exoderm. With regard to the mixed tumors it is very probable, however, that they can arise from disrupted embryonal germinal cells. Ribbert is of the opinion that this is particularly the case in sarcomas occurring in the very young.[2] Many of the tumors, particularly malignant tumors (glioma, teratoma, myosarcoma), would receive a satisfactory explanation of their histogenesis from the assumption that they grow from pre-existing dislodged embryonal cells. This is particularly true of tumors like carcinoma of the kidney developed from dislodged portions of the adrenal bodies. Ribbert assumes that these grow from portions of the adrenals which have been disrupted in an embryological state and continued to live in the substance of the kidneys. Such embryonal germinal cells may remain quiescent in the kidney parenchyma without forming a tumor, but under certain conditions which are not as yet thoroughly understood (Ribbert mentions hyperæmia), such cells undergo a rapid and progressive growth and multiplication. At first this is apparently a benign growth; it is well circumscribed and limited. But when it strikes a vessel and causes its

[1] Anatomisches Heft, I. Abth., Heft 9.

[2] Loc. cit., p. 606.

wall to atrophy by pressure, it proliferates into the vascular lumen and may even cause metastases. The important point to bear in mind in the case of this tumor is that there are precursory stages which are not carcinomatous, and that they may persist in this benign state indefinitely. Evidently some additional tumor producing agency is necessary here to convert the benign growth from dislodgement of adrenal cells into the parenchyma of the kidney into a malignant growth. It shall be our duty in the following to approach a solution of this question, whether or not an additional tumor producing agency is necessary to impart the character of malignancy to cells already in a state of proliferation.

Metaplasia. The transformations in form and structure which cells may undergo are important for the understanding of normal and pathological cell growth. Evidently if cells can change their specific structure and replace it by a different structure, which is, however, definitely differentiated or undifferentiated, it is not necessary to assume with Ribbert, that in all cases of mixed tumors we are dealing with disrupted or dislodged embryonal cells, as the starting point. Lubarsch's study of metaplasia suggests the possibility of the derivation of such tumors from metaplastic cells.

The *supposed participation of muscle, liver, cartilage and lymph gland cells* in the architecture of carcinoma metastases[1] are not genuine metaplasia—*i. e., transformation meaning the replacement of specific cell or tissue structure by other definitely differentiated structure of the same kind of tissue,* but they represent what Lubarsch cells pseudo-metaplasia, *i. e.*, the histological "cell accommodations" and "variations" of Hansemann—these are mere changes of form, not of structure. Naturally if the actual participation of the liver cells, etc., in carcinoma metastases derived from an original growth the stomach could be demonstrated, it would be a point gained for the advocates of the theory of infection for malignant neoplasms, but thus far their observations are cases of pseudo-metaplasia.

Lubarsch distinguishes three types of cell changes:

1. Pseudo-metaplasia—change in form but not of structure.

2. Metaplasia—structure transformation—replacement of specific cell or tissue structure by the different kinds of structure, but which is definitely differentiated and derived from the same type of tissue.

3. Undifferentiation—transformation of definitely differentiated cells into undifferentiated. Of this there are two types:

(*a*) Transient or physiological undifferentiation, occurring during progress of indirect cell division, during which typical structure is temporarily dissolved.

[1] Rindfleisch, Klebs, Gussenbauer, von Leyden, XX. Verhandl. d. Congress f. i. Med.

(*b*) Pathological (permanent) undifferentiation which always leads to death of cells by degeneration or atrophy.[1]

Ribbert seeks the cause of carcinoma in an inflammatory proliferation, which disrupts the cell from its physiological connection. The cause of the unrestricted growth of the cell is the removal of resistance to growth in the environment caused by the inflammation. This theory does not explain why a carcinoma does not occur in every instance where an inflammation disrupts cells from their normal environment, and why carcinomas actually develop in the absence of every evidence of inflammation. It is seen that all of these theories have some resemblance. They all attribute the malignant neoplasm to some undefined power of growth within the cell and differ only in regard to the reasons assigned to this power of growth.

A fourth theory, which is that of Hansemann, does not concern the etiology of malignant neoplasms, but only their morphology and physiology. His conception is expressed in the word "anaplasia." Hansemann first used the word "anaplasia" in 1890,[2] from *ἀνα*, backward, and *πλάσσειν*, to build. He understands by it a condition in which cells have lost in part their specificity, have become "entdifferenzirt," so that they have acquired the property of independent existence, have lost what he calls "altruismus." He conceives that this anaplasia is brought about by abnormal, especially unsymmetrical, mitoses, and that some of the "idioplasm"[3] is thereby lost, while idioplasm which had previously been in the background now comes to the front.

Difficulties in the Way of the Parasitic Theory of Cancer. Above all we must recollect that the controlling histological elements in carcinomas are the connective tissue and the epithelial cells. These cells are the element which cause the tumor by their multiplication and advancement, and generate the metastases by their proliferation in other organs. We do not find such a phenomenon in the parasitic diseases. In all parasitic diseases it is the micro-organisms which transfer the diseases and then make a new inflammatory focus out of the elements and cells of the newly infected organ. In a parasitic disease the tissues of the newly infected organ itself compose the inflammatory

[1] Benecke's "Kataplasia"—Hansemann's "Anaplasia." For fuller account see O. Lubarsch, Arbeiten a. d. Anat. Abtheilung, d. kgl. Hyg. Instit., Posen, S. 209, 1901.

[2] Virchow's Archiv., Bd. cxiv., p. 321.

[3] Idioplasm. In biology, a term introduced by Nägeli for a special hereditary reproductive substance not contained in the body of the cell, but in the chromosomes of the nucleus, controlling and determining the actual characters of the particular cell, and also those of all its descendants. Each idioplasm is composed of several or many *ids*, which are capable of growth and multiplication by division; although much smaller in bulk than the rest of the living substance of the cell or body (trophoplasm), idioplasm is the active element in the process of formation, and determines the detailed construction of the trophoplasm, which is the passive element.

tumor. In cancer the cells of the secondarily infected organ never participate in the metastasis, but this is composed exclusively of the cells of the organ primarily diseased. A primary cylindrical carcinoma of the stomach, when it causes a metastasis in the liver, never infects the cells of the liver, but the metastasis is composed of cylindrical stomach cells, or glandular epithelium from the mucosa of the stomach. This is true of other metastases. In no infectious disease do we find that cells from the primary focus of inflammation are driven about, nor do such cells of infectious diseases cause characteristic new-growths histologically like themselves in other organs.

1. The parasites must live within the cell, and yet not injure it, in order to make the parasitic theory harmonize with the well-ascertained morphological facts concerning cancer proliferation. We must assume, then, a kind of symbiosis of parasite and cell. At the same time they must be able to bring into disorder the various finer cell parts already considered, in order that the incentive to cell proliferation shall be present. Whether such parasiticism is possible is doubtful.

2. As the unrestricted proliferation of the cells, as well as the power to form metastases, is ascribed to the presence of the parasites within the cells, it is necessary to assume that every cell contains a parasite, and that the parasite multiplies as rapidly as the cell, in order that each new cell shall receive its parasite. If the parasites do not divide in the identical moment that the cell divides, cells will eventually arise which contain no parasites, and, therefore, have no abnormal properties in the sense of the adherents of this theory. This condition necessitates that the cycle of development of the parasite should coincide with the rate of multiplication of the proliferating cells.

3. The best evidence points to the conclusion that transplantation of malignant neoplasms is successful only among animals of the same species. A parasitic disease, however, if we are permitted to draw inferences from the well-known infectious diseases, should be transferable from one species to another.

4. Primary carcinomas rarely occur in multiplies; only in exceptional cases of epithelioma of the skin has this been reported. Typical congenital malignant neoplasms (rhabdo-myosarcoma of the kidney, glioma of the retina) have been reported in children whose parents were not affected with malignant neoplasms.

5. The cells of organs invaded by cancerous metastases do not participate in the secondary growths. The metastases, with few exceptions, represent the cell type of the mother carcinoma.

6. Cells of a different type, then, being only exceptionally involved in the metastases, it is necessary to assume that every kind of cancer must have a special species of cancer parasite, which would not be capable of causing cells of another type to proliferate in a cancerous

manner. A pavement epithelial cell of the œsophagus, for instance, when it causes a metastasis in the stomach, produces a neoplasm composed of pavement epithelium; never cylindrical cell growth or an adenocarcinoma—structures which are found in the normal gastric mucosa.

ATTEMPTS AT EXPERIMENTAL PRODUCTION OF CARCINOMA. The special object of this report is to communicate in abstract a series of researches or efforts aiming at an experimental production of carcinoma of the stomach. This organ is more than all other organs in the body fitted for a study of cancer because it is more frequently invaded by this disease than any other organ or tissue in the body.[1] Not only this, but it is the only organ of which it is definitely known that a benign lesion, the peptic or gastric ulcer, may exist as such for months or even years and then can undergo changes transforming it into a typical malignant neoplasm. The scientific value of any series of investigations on cancer will depend very much upon the experience and familiarity of the investigation with the architecture and pathological physiology of these growths. It is for this reason chiefly that I confined my experimental studies to the adenocarcinoma of the stomach, believing that I could not be misled in confusing this characteristic growth with any of the other neoplasms of the stomach, or with simple inflammatory tumor. (See Hemmeter, *Diseases of the Stomach*, 3d edition, p. 527 to 586, on "Malignant Tumors of the Stomach.")

Gastric carcinoma may develop from the oxyntic or parietal cells (gland cells) of the peptic ducts, when they constitute the adenocarcinomas; but they may also arise from the cylindrical epithelium of the vestibules, and then they are termed cylindrical cell carcinomas; and finally, they may develop from the mucous glands; if the adenocarcinoma is restricted to the mucosa and grows outward, the stroma is composed of newly-formed connective tissue—if the carcinoma grows in the main muscular layer the stroma may be muscular tissue.

In 1898 I began with experiments attempting the transplantation of pieces of adenocarcinoma from the human stomach into the stomachs of dogs, cats, and guinea-pigs. I have a record of forty-two such attempts, but in not one case have I succeeded in successfully transplanting a piece of human concer of the stomach into the stomachs of any of these animals.[2]

In the *Journal of Medical Research*, vol. vi., No. 1, and vol. viii., No. 1, Dr. Leo Loeb describes the transplantation of tumors (sarcoma)

[1] The literature and statistics on this subject will be found compiled in a volume by Behla, "Die Carcinomlitteratur" (up to 1900), pages 244 and 248.

[2] The literature on transplantation of cancer from man to animals is compiled in "Ueber die Aetiologie des Carcinoms," by Gustav Fütterer, Wiesbaden, 1901. It appears from this compilation that 11 experimenters claimed to have had successful transplantations, but 19 others had negative results. A number of other transplantations are mentioned and criticised in Hansemann's work, loc. cit., p. 174.

through forty generations respectively of rats of different age and sex. In all cases a sarcoma was produced, and the details of the growth and generative changes of the cells were preserved. Even certain limits of variability in the cells were also preserved. Dr. Loeb assumes it to be a well-known fact that transplantation of cells[1] into animals of different species are usually unsuccessful, and this may account for the impossibility of producing a tumor in another species. The sarcoma which he found in the connective tissue of the parathyroid could never be successfully transplanted into any other species of animals. Guinea-pigs, animals so susceptible to tuberculosis of different origin, remained absolutely unaffected by these tumors. He suggests that certainly none of the ordinary micro-organisms can be the cause of these new-growths, of which there was no doubt that they were true sarcomata.[2]

In a more recent contribution, Mayet[3] reports transplantation experiments, in which he introduced pieces of human cancer into animals subcutaneously, or by rubbing up pieces of human carcinoma with sterile bouillon, and injected the resulting emulsion into the peritoneal cavity, or into the circulation of animals. Most frequently, however, he injected a glycerin extract of human cancer tissue, aseptically macerated, or a filtrate obtained by filtering such crushed tissue through a Pasteur filter or an asbestos filter. Previously, the animals used received cantharidin injections, with which he aimed to produce transitory nephritis and so to predispose the kidneys to the development of cancer nodules. Mayet experimented on dogs, rabbits, and white rats. He admits that his experiments on dogs and rabbits were unsuccessful, but claims that he succeeded in certainly producing cancer lesions in three white rats out of fifty-three of these animals experimented upon. These alleged successful cases he claimed were produced by the glycerin extracts or filtrates from human carcinoma. A critical study of Mayet's paper leads one to be especially skeptical concerning his claim of having produced a genuine carcinoma in this manner. He does not describe the typical architecture of a carcinoma, but speaks of epithelial cancerous lesions.

An interesting series of experiments on tumor transplantations and inoculation is described by Dr. M. Herzog.[4] The original animal which Herzog used was a descendant of the white rat from which L. Loeb[5] derived his sarcoma. The growth was a vascular cystic sarcoma of the thyroid in a rat. Over fifty successful transplantations were made in the

[1] The literature on the transplantation of cancer cells from animals to animals is compiled in the work of Fütterer, Behla, Hansemann.

[2] Loc. cit., p. 49.

[3] "Production du Cancer chez les Rats blancs Introduction dans leurs Economies des Substances constituantes des Tumeures malignes de l'Homme?" Gaz. hebdom. de Medic. et de Chir., January 19, 1902, No. 6, p. 64.

[4] Journal of Medical Research, vol. viii., No. 1, p. 74.

[5] Loc. cit.

same species of animal, and these extended over eight tumor generations. In the inoculation experiment of Herzog, pieces of non-infected sarcoma were ground up in a sterile mortar with sterile quartz sand and silicon powder. The tissues were ground up with physiological salt solution—the emulsion so prepared filtered through a Pasteur filter, and the filtrate so prepared inoculated into culture tubes, showing it to be free from micro-organisms. Several cubic centimetres of this filtrate were injected into the abdominal cavity of rats—not a single one of the rats so treated developed a tumor. Some were killed and examined, and the findings were absolutely negative. Thus far Herzog's investigations are clear and instructive; but further on he mentions the possibility of ultra-microscopic organisms, too small to be seen even by the aid of our best optical instruments. He claims that bovine pest can be propagated by filtrate through a Pasteur filter, and that the work of Nicolle and Abdil Beyer gives evidence that the cause of this disease must be a living organism which can pass through a Pasteur filter. I am not sure that the work of Nicolie and Abdil Beyer justifies such a conclusion.[1]

I have given these previous experiments such detail because they express in the work and words of others much of the work and experiment which I have made personally, yet never published. I have also prepared a sterile filtrate of human carcinoma of the stomach, exactly in the manner as described by Herzog, and injected it into the stomach tissue of dogs, cats, and rabbits, but never succeeded in causing a gastric malignant neoplasm in these animals by this process.

It is a well-known fact of pathology that the human gastric or peptic ulcer may become transformed into an adenocarcinoma, apparently spontaneously. This process has been described in a classical investigation by Hauser.[2]

In 1900 I paid a visit to Professor Hauser's laboratory at the University of Erlangen, and was fortunate enough to see some of his original preparations and sections. I have also had a rather exceptional clinical experience with cases of gastric ulcer in the human being, which I had studied, in one case, for over two years, during which it presented the typical clinical history of gastric ulcer. Then followed the clinical history of gastric carcinoma and death.[3] Naturally, the question arose in my mind, "*If gastric ulcers could be produced experimentally in animals, their transition into possible adenocarcinoma might be studied at*

[1] As far as I know the experiments of L. Loeb and M. Herzog have not been confirmed by others, nor am I in a position to judge whether the neoplasms they claim to have produced were genuine sarcomas.

[2] Das chronische Magengeschwür, sein Verharbungs-Process und die Beziehung zur Entwickelung des Magencarcinoms," Leipzig, 1883; and "Das Cylinderepithelcarcinom des Magens und des Dickdarms, Jena, 1890. See, also, New York Medical Record, 1897, vol. lii. p. 365; also, Hemmeter, "Diseases of the Stomach," third edition, p. 560.

[3] See Hemmeter, New York Medical Record, 1897.

will, or the transformation into adenocarcinoma might be attempted by the transplantation of malignant neoplasms derived from other animals of the same species, or by the injection of sterilized filtrate of ground-up adenocarcinoma of other animals of the same species into the tissues surrounding the edge of the ulcer."

Among the causes that are definitely ascertained as contributing to the bringing about of gastric ulcer are especially three:[1] first, impaired vitality or injury to the mucosa of the stomach; second, hyperacidity or supersecretion of gastric juice containing an excess of HCl, and proteolytic ferments; third, an altered or impaired state of the blood.

All three of these factors may be produced artificially, and when we do produce them in the laboratory on animals, peptic ulcers arise in such a large proportion of the animals thus experimented upon, that we have a right to conclude that they are directly attributable to the method pursued. When I speak of peptic gastric ulcer I mean the typical "chronische magengeschwür" as described by Hauser. For defects can be produced in the dog's stomach, for instance (and the literature on the experimental production of gastric ulcer proves this conclusively), which are not true gastric ulcers, but simply ulcerating lesions, which heal rapidly. Gustav Fütterer has produced such lesions by applying to the stomach caustics, ligating the gastric arteries, cutting off the supply of nutrition by stitching large portions of the mucosa with catgut sutures. Defects resulted, but they all healed in a short time. Even when one-third of the quantity of the animal's blood was withdrawn such defects had healed in two weeks. In 1896 Silbermann[2] produced gastric ulcers in dogs by either tying the gastric arteries or causing emboli in them by injecting suspensions of lead chromate. Thereafter he injected hæmoglobin and pyrogallic acid. When Fütterer resected the gastric mucosa, as stated before, and made injections of pyrogallic acid, he could confirm Silbermann's results, and produced ulcers of the stomach which in every histological detail corresponded to the chronic gastric ulcer of the human being. By making use of this method employed by Fütterer and Silbermann I was successful in producing experimentally gastric ulcers in one series of experiments; eleven dogs out of thirty operated upon developed typical gastric ulcer.

Now I had a method by which this characteristic lesion could be produced experimentally. The next question was, "Could these lesions be in any way experimentally transformed into adenocarcinoma of the stomach, or could they become transformed into adenocarcinoma spontaneously, as has been definitely known to occur in the human being,

[1] See Hemmeter's "Diseases of the Stomach," third edition, p. 491.

[2] Experimentelles in klinisches zur Lehre von Ulcers Ventriculi rotundum. Deutsch. med. Wochenschr., 1886, No. 29, p. 497.

and as Fütterer has observed, to occur in a rabbit, in which he had artificially produced a gastric ulcer by the method described?"[1]

Hauser has described a structural characteristic of the adenocarcinoma of the stomach, which had developed on the basis of a gastric ulcer, and which is not observed in ulcerating carcinomas not developed on this basis. This characteristic by which the so-called "ulcus-carcinomatosum" can be recognized, consists in a very peculiar behavior in the fibres of the chief muscular layers of the stomach, and also of the fibres of the muscularis mucosæ. This peculiar behavior of the muscularis consists in an oblique ascension of the fibres of the true muscular layer, and a descension of the fibres of the muscularis mucosa, the fibres of both muscular layers converging toward and fusing into each other in front of the edge of the ulcer, which is here composed mainly of connective tissue. The true muscularis bends upward in continuity, and the border of the ulcer, which is composed of very dense connective tissue, is limited by the lower or peritoneal strata of the turned-up true muscularis.

Another feature of the ulcus carcinomatosum is that a section made perpendicularly to the surface of the stomach, and through the entire bed of the ulcer, almost invariably exhibits the general outline of a fish-hook.[2] For the causes which bring about this fish-hook formation,[3] the main reason being that the lower edges of the ulcer near the pylorus are, during the efforts of gastric peristalsis to evacuate the chyme into the duodenum, exposed to the most mechanical irritation, and, accordingly, Fütterer has shown that adenocarcinoma, if it develops from an ulcer, always develops from the lower edge. This location for the development of gastric ulcer had already been emphasized in a publication by Dr. Delano Ames and myself, but it is the merit of Fütterer to have emphasized this point as an etiological factor in the causation of ulcus carcinomatosum.

I should add that in repeating the experimental production of gastric ulcer, according to the methods of Silbermann and Fütterer,[4] I not only produced mechanical defects, and injected pyrogallic acid in the method described, but I maintained a very high acidity for free HCl in the gastric chyme of the dog by supplying this acid in his food and also pouring it into his stomach through a soft rubber tube. In February, 1900, I came into the possession of a mongrel fox-terrier, who persistently vomited his food. The vomit contained no free HCl or ferments, and at the autopsy a cancer of the stomach was found near the pylorus. Transplantations with this material were made into the stomachs of other

[1] Loc. cit., p. 152.

[2] See Hemmeter, "Diseases of the Stomach," third edition, plate ix., opposite p. 506; also New York Medical Record, loc. cit.

[3] Loc. cit., p. 112.

[4] New York Medical Record, September 11, 1897.

fox-terriers, but I was not successful in producing a gastric carcinoma in any other animals inoculated.[1]

In the meanwhile the publication of Fütterer appeared, and it occurred to me that possibly my failure to successfully transplant canine carcinoma was due to the fact that the stomach of the animal into which the inoculation was made was not in a susceptible condition, and that it must be transformed into such a condition by a previous injury. This previous detriment to the tissue, in order to secure successful transplantation of the tumor, has in the case of rats not been found necessary by Leo Loeb and M. Herzog. I did not succeed in securing another dog affected with carcinoma of the stomach until after I had read Fütterer's work in 1901, and this second dog presented an adenocarcinoma which developed spontaneously at the edges of an experimental gastric ulcer. It presented the behavior of the two layers of the gastric muscularis, as first described by Hauser, had a distinct fish-hook form, and exhibited heterotopia of gastric glands, as first described by Virchow[2] and Hansemann.[3] This gastric cancer reached the size of a walnut, and two metastases were found in the omentum. It was this carcinoma which was used in making a filtrate with which the edges of the peptic ulcer previously produced in other dogs were injected.

It will be seen that these experiments are attended with unusual difficulties in procuring the material, for if we wish to study the effect of extract of adenocarcinoma upon experimentally produced gastric ulcer, we must have two sets of animals: one presenting the cause and the other the gastric ulcer. If we should accidentally come across a dog with an adenocarcinoma it would take at least two or three weeks to get a number of other dogs having experimental gastric ulcers. It is a matter of great difficulty to determine in the live animal whether it is really afflicted with gastric cancer, and if the cancer is accidentally found at autopsy in a veterinary school, it rapidly decomposes, and unless kept on ice the canine gastric cancer becomes useless for experiments in two or three days, for bacteria, especially the pus cocci, are great hinderances to successful transplantation, as Loeb[4] has emphasized. We will, therefore, in future, have to depend on cancer tissue gotten from living dogs, or soon after the autopsy, or such cancer tissue produced experimentally by the method of Fütterer, which in my experience only succeeds in one-third of the animals experimented upon.

[1] Sepsis followed a large proportion of the operations, and I could not secure the aid of a competent surgeon who would do these operations aseptically for me. A sterile extract of part of this canine carcinoma was also made and prepared for inoculation and injections into dogs, in which I expected to cause gastric ulcers. A very small quantity of filtrate (48 c.c.) was thus saved, as the largest part of the tumor had been used for transplantations.

[2] Virchow's Archiv., Bd. 111.

[3] Loc. cit., p. 195.

[4] Loc. cit.

The adenocarcinoma which developed at the edges of the experimental peptic ulcer was found at a time when I was engaged in producing such ulcers in a series of animals. Eight transplantations of such tumor particles were made into the edges of peptic ulcers of other fox-terriers. Five of these animals died of infection and other intercurrent accidental complications. Three of them lived each three months after the transplantation, and of these three, two had developed adenomatous proliferations closely resembling carcinoma at the edges of the gastric ulcer nearest the pylorus.

SUMMARY. Eight dogs afflicted with experimental peptic ulcer, inoculated by injecting tumor particles made of suspension of the tumor cells of a gastric adenocarcinoma into the edges of the gastric ulcer. Five of these animals died of sepsis, etc., three of them lived three months each, developed symptoms of gastric carcinoma, and in two of them the adenomatous proliferations described by Hauser and Fütterer were evident at the pyloric edge.

This method of inoculation by a suspension of the tumor cells was preferred to transferring actual pieces, because I had a very small original tumor to start with, and for the purpose of demonstrating the principle involved, it makes no difference whether we transfer large pieces or only a few cells, for any ensuing development of carcinoma can only in these cases be attributed to a further growth of the injected carcinoma cells, or whatever hypothetic micro organism or tumor producing agency they may be assumed to carry. My main object, however, was to discover whether the cancer formation at the edges of gastric ulcers could be induced by the injection of a fluid gained from canine carcinoma and free from carcinoma cells as well as micro-organisms, as far as our modern methods of testing these two points permit us to judge.

PRODUCTION OF EFFORTS AT ADENOMATOUS PROLIFERATION FROM THE EDGES OF PRE-EXISTING EXPERIMENTAL GASTRIC ULCER BY THE INJECTION OF CELL-FREE AND STERILE EXTRACT OF CANINE GASTRIC ADENOCARCINOMA. The sterile and cell-free extract of canine gastric adenocarcinoma was prepared by grinding up non-infected portions of this cancer in a sterile mortar with quartz sand, together with physiological salt solution. Then this emulsion was filtered through a Pasteur filter, and cultures made upon a number of the most commonly used media, which proved negative. In order to exclude the possible action of bacteria, I might of course have used strong antiseptics in the solution, such as bichloride of mercury, formaldehyde, carbolic acid, etc. There are, however, two grave objections to this way of proceeding. I shall have to premise what I intend to say by stating that I had from previous observations and experiments gained the impression that the tumor producing agency in these cases was not the cell itself, nor a

micro-organism, but an enzyme, which had passed through the filter. The first objection to using antiseptics or heat in sterilizing the filtrate was that whilst they no doubt could destroy any micro-organisms, a sufficient degree of heat, as well as the more effective antiseptics, would also destroy any possible enzyme present. The second objection to using these substances was that any possible effect upon transforming the peptic ulcer might have been ascribed to the antiseptic use or to chemical additions to the filtrate and not to any inherent qualities derived from the original tumor. I have, however, shown that thymol, even in saturated solution, has no such destructive action upon the proteolytic ferments of the intestinal canal.[1]

A. S. Loevenhart and Kastle, in their beautiful investigation on the reversibility of the action of lipase[2] and Loevenhart in his researches on lipogenesis[3] toluene was used to keep the tissue extracts sterile, and evidently the effectiveness of lipase was not impaired by this antiseptic. In one of my successful experiments I also made use of toluene, and I believe this excluded the possible action of any bacteria that might be presumed to pass through a Pasteur filter. From the investigations of William G. Wherry[4] concerning the permeability of the Berkefeld and the Pasteur-Chamberland filters to bacteria of small size it seems justifiable to conclude that bacteria of small size can pass through them. The bacillus producing pneumonia in guinea-pigs, for instance, will pass through the pores of a small Berkefeld filter, No. 5, and sometimes organisms which do not pass through the above filters, like the bacillus coli communis, may grow through. Referring once more to the work of Herzog, it seems justifiable to conclude from the results of Wherry, that if the virus of a disease passes through the pores of a Berkefeld filter, it is not necessarily ultramicroscopic. The practical import for our research was that we could not rely exclusively upon filtration, but had to resort to some antiseptic in order to attain an absolutely sterile liquid. For this purpose thymol, and in some cases toluene, were used.

As far as the methods at present at our disposal permit me to judge, the filtrate extract used for these inoculations was sterile. The injection of filtrate into ten animals afflicted with experimental gastric ulcer resulted in four of them in the development of adenomatous proliferation closely resembling an adenocarcinoma at the edges of the ulcer. The time in which the animals were examined after the first injection varied

[1] Hemmeter, "Ce que Deviennent les Ferments Digestifs—Bacteries proteolytique du Colon," XIII. Congres International de Médecine, Paris, 1900, also "Ueber das Vorkommen von Proteolytischen und Amylolytischen Fermenten in Inhalt des Menschlichen Kolons," Pflüger's Archiv. f. die ges. Physiologie, Bd. 81, 1900.

[2] American Chemical Journal, xxiv., 1900.

[3] American Journal Physiol., vol. vi. p. 331.

[4] Journal of Medical Research, November, 1902.

from twelve to fifteen weeks after the first injection. The histological characteristic of the carcinomas developed corresponded closely to those described by Hauser and Fütterer: (1) There was a diffuse proliferation of glands; (2) heterotopia of gland cells; (3) the cells of the proliferated gland ducts stained apparently as deeply as the normal cells in the same section; (4) there were numerous mitoses in the proliferated gland cells, some of them atypic, and also mitoses in the connective tissue cells close to the proliferated glands. Notwithstanding these histological characteristics, I am by no means of the opinion that the proliferation produced in this way was really a malignant neoplasm, for I have observed such proliferations around two peptic ulcers that were excised by operation, and the patients remained well eight and nine years respectively.

The question arises if the adenoma thus produced was not caused by the implantation of a carcinoma cell, nor by infection with bacteria, what did cause it? This question opens a wide field for reflection. If the Pasteur filter can keep bacteria as well as cells from passing through, the incentive to growth can only have been given by some chemical substance capable of passing through the filter, and contained in the filtrate. This substance was extracted from a pre-existing carcinoma in a dog. But it is essential to bear in mind that in one case the gastric ulcer developed into a carcinoma spontaneously. Evidently the cellular tissue of the stomach, in its abnormal condition, is capable of producing in itself the tumor forming agency, and whatever a tissue can produce out of its own cellular structure, if it can be proven that the tumor producing agency is not a bacterium, must be a product of the cells themselves, and very probably inherent in the cells.

Comparisons of the Relative Osmotic Pressures of Normal Cells and Carcinoma Cells of the Same Organ. Normal cells, as well as carcinoma cells, can be isolated from their stroma by pencilling portions of fresh tissue in salt solution, isotonic with the blood plasma. The strength of this solution will vary with different animals. The serum of human beings is, according to H. J. Hamburger,[1] isotonic with a 0.84 to 0.89 per cent. solution of sodium chloride. I have observed cells from a carcinoma of the stomach in such salt solution on the warm stage, and compared them with the cells of normal stomach tissue. Whilst there was no apparent change in the normal gastric cells the gastric carcinoma began to contract in the course of the day, four to five hours, as if they were in an hyperisotonic solution. Not all cells of gastric carcinoma that are pencilled out in an isotonic salt solution will show this contraction. One notices that in perhaps one-fourth to one-

[1] Osmotischer Druck und Ionenlehre, p. 445.

third of the cells there is no contraction evident. I have gained the impression that although carcinoma cells represent cells that are emancipated from the laws of normal proliferation (if I may speak of such laws), nevertheless the carcinoma cells themselves, although alienated from the general cell state, may be healthy or diseased. By healthy in this sense I do not mean that they are normal cells; but simply that they represent a condition of the cells as occurs in the majority of cancers before they begin to disintegrate. When a cancerous tumor undergoes necrobiosis certain of its cells undergo a still further pathological process and it is in these cancers undergoing cellular destruction in which the perfect lawlessness of the cancer cell becomes manifest. I am of the opinion that those cancer cells which do not act like the majority in isotonic salt solution are perhaps already undergoing the beginning changes of necrobiosis. The majority of cancer cells show a contraction, whereas this minority does not show this phenomenon. Difference in staining of the protoplasm and chromosomes can also be observed in these two kinds of cancer cells. I am in doubt whether this phenomenon of contraction or swelling, as the case may be, would be possible in the cells of all types of cancer. The adenocarcinoma of the stomach is derived from an epithelial and glandular cell which even normally gives evidence of marked regenerative power. It possesses marked mutability, as Virchow would say, and these powers are still manifest when this cell becomes emancipated from the normal laws of proliferation. I have not been able to try the experiment, but I doubt whether the cells of an osteoma, chondroma, or scirrhus would be capable of undergoing visible osmotic changes under the microscope, no matter how different the osmotic tension of their environments would be made from the tension existing within their protoplasm.

Similar observations were made with the cells of a mammary carcinoma, comparing their behavior to that observed on normal mammary gland cells in isotonic solution. I have also compared the behavior of normal gastric gland cells with those of a gastric adenocarcinoma after they had been pencilled out in the blood plasma of the same patient, and also in the blood plasma of another but normal individual. The same differences were found between the two in blood plasma as observed in isotonic salt solution. These studies led me to suspect that a deep-seated disturbance exists between the osmotic tension of the living cells of a cancer and the surrounding juices, mainly because the cancer cells act differently from the normal cells of the same tissue when placed in the same isotonic solution or in blood plasma of the same individual. Thus far these studies have been made only in mammary and gastric adenocarcinoma, and I would caution against the extension of the observations to all forms of tumors until these have been thoroughly studied in this way. It must be emphasized here that as

these pieces of tissue could only be gained at operation, I was restricted in my search for normal cells to tissue in the immediate neighborhood of the malignant growth. It is probable that cells of the same organ, more remote from the malignant growth, might have shown a still greater contrast. I am now studying the behavior of normal cells observed in cancer juice expressed from a cancer of the same organ. Normal cells of an organ observed in such cancer juice will give evidence of swelling in the course of three to five hours. These phenomena might be interpreted by differences in osmotic tension between the protoplasm of the cell and the surrounding solution. For instance, if a normal cell swells up in filtered cancer juice, we may be correct in assuming that it takes up water, that the cancer juice contains relatively more water than the protoplasm of the cell. Increase of volume of the cell, if associated with cytolysis, may be due, however, to the presence of toxic substance in the cancer juice. This has at present not yet been satisfactorily investigated. The fact that the majority of healthy cancer cells contract in salt solution isotonic with blood plasma would indicate that they have lost water. It is justifiable to assume that the osmotic tension between a cancer cell and the normal cancer juice as existing in its environment is isotonic, for a cancer cell will not change its volume in cancer juice. However, in the production of this juice it is unavoidable that the cancer cells are cut and bruised and considerable of the cytoplasm of the cancer cell may be contained in it, which is not present in the juice bathing the cancer cells in the ordinary state of these growths. Material is very difficult to obtain, for although the cancer tissue is readily obtained from operators, they do not, as a rule, cut far away from the limit of the growth into the normal tissue in an effort to remove it.

These are purely physical conditions, but they show a definite disturbance of osmotic tension.

Phenomena of cell division are as Bütschli, Quincke, and Jacques Loeb believe, phenomena of protoplasmic streaming. They require, as Quincke has shown, a definite degree of viscosity. We have to remember that all life phenomena, normal as well as abnormal, are ultimately due to motion, or changes occurring in colloidal matter.[1] No protoplasmic motion can occur if the normal viscosity of this matter is disturbed in either direction, that is, if it is too great or too small. It may be that the disturbances in osmotic pressure, which I have suggested in the preceding, may lead to changes in the viscosity of cell protoplasm, either favoring or inhibiting cell division.

Changes in Volume Which Normal Cells Undergo in Cancer Juice. Studies on osmotic pressure made by means of the hematokrit,

[1] Jacques Loeb, "The Comparative Physiology of the Brain, etc., p. 14.

according to the methods of Hedin[1] and Köppe,[2] indicate that normal cells of the stomach or mammary gland cells when placed in cancer juice derived from a gastric or mammary cancer, swell up as if they were in a hypisotonic solution. The red blood cells of normal human beings and also of cancer patients will lose some of their coloring matter when placed in sterile cancer juice or sterile filtrate made as described in the preceding portion of this article. This would, in some of my studies, occur even when this filtrate or cancer juice was made isotonic with the blood plasma, and is suggestive of a substance in the cancer juice which is capable of making the stroma of the blood corpuscles permeable to toxic or other substances capable of effecting dissolution of the hæmaglobin; and reminds one of the experiments of Belfante and Carbon,[3] and also those of J. Bordet.[4] These experiments demonstrated that toxic substances are formed in the blood serum of animals into whom blood of another animal species had been injected. If the blood of a rabbit is injected into the peritoneal cavity of a guinea-pig, the serum of the guinea-pig blood will acquire the property of destroying the red blood corpuscles of rabbits, a property which the serum of normal guinea-pigs does not possess. If 5 c.c. of serum of a normal guinea-pig are injected into the circulation of a rabbit, this animal is in no way influenced thereby. But if this serum is derived from a guinea-pig which has previously received several injections of rabbit blood, then it becomes dangerous to a rabbit. A few minutes after the injection the rabbit dies and the autopsy reveals extensive dissolution of the blood and numerous hemorrhages as a consequence. Similarly the blood of the guinea-pig can be made to acquire a destructive property upon cholera bacteria after a small amount of a culture of cholera vibrios have been injected into the peritoneal cavity of the guinea-pig. Ehrlich and Morgenroth[5] and the other authors agree that this hæmolytic and bacteriolytic action of guinea-pig serum is due to two substances, one of which they speak of as a "sensibilisator," and the other as an "alexin." It is the penetration of the "alexin" into the red blood corpuscles which makes it lose its coloring matter, but this "alexin" cannot work unless the blood corpuscles have been sensibilized by the other agent. The "sensibilisator" is formed in the circulation of the guinea-pig by the intraperitoneal injection of rabbit blood. The "alexins" are normally present in the circulation of the animal. It was discovered that the sensibilizing substance can tolerate a temperature of 70° C. without destruction, but that the "alexin" is destroyed at a tempera-

[1] Skandinavisches Archiv. f. Physiologie, 2, 134, u. 360.
[2] Dubois-Raymond's Archiv., Physiol. Abt., 1894, 154.
[3] Referred to by Metschnikoff, Annals of the Institut Pasteur, June, 1900, No. 6, p. 370.
[4] Ibid., October, 1898, April, 1899.
[5] Berliner klin. Wochenschr, 1899, Nos. 1 and 22.

ture of only 55°. I have said that the normal serum of the guinea-pig contains "alexins," which are preserved, of course, in the serum made active against the blood corpuscles of the rabbit. If the active guinea-pig serum is heated to 55° the "alexin" is destroyed, but the sensibilizing substance remains active. In such a serum the rabbit blood corpuscles retain their coloring matter, for the "sensibilisator" is not capable of producing hæmolysis. But as soon as serum from a normal guinea-pig or a normal rabbit is added, the coloring matter of the blood corpuscles begins to part from the red blood cells, for both the normal guinea-pig as well as rabbit serum contain "alexin." These agents which produce hæmolysis partake of the nature of catalytic agents. Ehrlich and Morgenroth speak of "*Zwischenkörper*" (intermediate bodies), and also of "*complement*." In none of these investigations is it stated that these substances have been isolated.[1] The speculations concerning them are based exclusively upon an observation of their effects. They were important for me, however, in suggesting the idea that perhaps the cell growth representing cancer might in some way be associated with the influence of a catalytic agent which could be studied in a similar manner by its effects on the normal cells of the same tissue or upon the blood cells of the same or normal individuals. The effects which I have observed of cancer juice on normal cells of the same organ, and of cancer juice and cancer filtrate upon blood corpuscles, throw no direct light upon the pathogenesis of malignant growths. They were undertaken merely because such studies had, to my knowledge, not been undertaken heretofore, and I felt that I was following the injunctions of Julius Robert Mayer that a phenomenon should be studied from every possible aspect before we should seek consolation in an hypothesis. Then again there was the hope that some reaction might be discovered whereby we might be enabled to tell what was a malignant growth and what was not, by the effects of the juices of a malignant growth upon normal cells. This has, so far as my work is concerned, not as yet been successful. The question is so manifold and the liability to error in whatever direction one goes is so great, that no practical conclusions should as yet be drawn. A weak point of these investigations consists in the fact that the juices and filtrate extracts of benign growths have not as yet been studied in their possible action upon cells of the same organ, or upon blood cells, nor even have the tissues and filtrate extract of normal tissues in their actions upon each other been studied satisfactorily. The question might be asked, "Does the tissue of an entirely normal stomach contain an agent concerned in the cell growth of gastric tissue which on being extracted from a whole stomach, concentrated by aseptic evaporation, and injected into normal

[1] I shall apply the inspiration gained from the work of Bordet, Ehrlich, etc., in the explanation of the rarity of metastases, under the heading of "Metastases," later on.

gastric tissue of another animal of the same species, will cause increased growth of that tissue?" For the development of the growth of the mucosa we would have to limit ourselves entirely to extracts of the mucous membrane, for the stomach contains layers of widely different cellular structure. If such an extract of mucosa does not affect the normal stomach would it cause cell proliferation after being injected into the edges of a gastric ulcer? As the difficulties of this investigation seem almost insurmountable, depending largely on procuring proper and abundant material, I have given expression to these suggestions with the hope that they may be of value to other investigators.

This much I will have to emphasize, "Whatever the substance or agent may be which causes a benign canine gastric ulcer to be transformed into an adenoma," it is destroyed when the filtrate is heated to 60° C. (140° F.); for while four animals out of ten injected with the unheated filtrate developed adenoma, no such result followed in six animals afflicted with gastric ulcers when they were injected with the filtrate that had been heated to 60° C.[1]

Problems of Cell Growth. All of these questions are intimately related with the *problems of cell growth*. The immediate and specific causes of cell division are still imperfectly known. Is cell proliferation due, as Ribbert[2] thinks, exclusively to the removal of inhibition or restrictions to growth in the environment of the cell, or is it due to proliferative forces within the cell? We have thus two conceptions of the immediate causes of cell growth, one without and the other within the cell. According to Thiersch and Boll, each tissue continues to grow up to the limit afforded by the resistance of neighboring tissues or organs. In the fully developed body the mutual relations of the cells are of such a nature that the conditions for further proliferation are unfavorable. Ribbert and others express this in the term "tissue tension" ("*Gewebe spannung*"), which prevents an increase of growth in the cells. They understand by this "tissue tension" all the mutual influences of the tissue constituents upon each other; they do not exactly mean mechanical pressure, although this no doubt plays an important rôle in restricting growth. The removal or lessening of this resistance to growth through injury or disease causes the resumption of growth and cell division, leading either to regeneration of lost parts or the formation of abnormal growth. According to the precedent of Virchow, it was formerly held that not only the function of a cell, but also its growth could be directly caused by the action of external stimuli. Virchow distinguished, accordingly, between functional, nutritive, and formative stimulation. This doctrine

[1] I am refraining from designating the proliferation as carcinoma for reasons given at end of article.

[2] Loc. cit., p. 300.

was contested by Weigert, whose efforts to disprove the power of external agencies to stimulate directly cells to proliferation have been very instructive. Weigert postulates that some primary injury to the tissues, as the immediate effect of chemical, mechanical, and other external agencies, is necessary to stimulate growth. This postulate has been fulfilled in many instances where such a cell injury had not been previously suspected. Better methods of investigation will no doubt enable us to demonstrate such an injury to the tissues. At the same time it is going too far, in my opinion, to attribute all morbid cell growth to such cell injury. In a comprehensive way Weigert's theory may be stated as follows: Cells are incited to growth through removal of obstacles to growth in the environment, in consequence of some disturbance in the normal relations or equilibrium of the cells with surrounding parts. The capacity of cells to proliferate has become latent when a certain "tissue tension" has been reached; it has become potential by the establishment of definite relations between cells themselves and between the cells and the basement substances, bloodvessels, lymphatics, tissue juices, and chemical substances contained in them.

We have hitherto studied cell growth as conceived to be due to a removal of restriction to proliferation outside of the cell body. In all these cases, however, it is difficult to determine the immediate stimulus to cell division, for a long chain of causes and effects may intervene between the primary disturbance and the ultimate reaction of the dividing cells. The opinion is gaining ground that the immediate causes of cell proliferation, whatever their antecedents, are to be sought in local chemical changes. Recent experiments on the proliferation in the ova of various invertebrates, conducted by Jacques Loeb, T. H. Morgan, R. Hertwig, and Mead, give ground for the conclusion that the stimulus to cell growth is of a chemical nature.[1] The climax of these experiments is reached in Loeb's artificial production of parthenogenesis in sea-urchin eggs by treatment with dilute magnesium chloride. The remarkable gall formation in plants leaves no doubt that extremely complex abnormal growths may result from specific chemical stimuli, and pathologists have held that abnormal growth in the animal body may also be incited by abnormal local chemical conditions. Only in two ways, then, can the cell be incited to growth—either by the removal of resistance to growth in the environment or by an increase in the formative energy resident within the cell. William H. Welch[2] concedes both of these possibilities—*i. e.*, forms of energy acting from without directly increasing the formative energy of the cell, and stimulating it to growth and multiplication; and, secondly, increase of the proliferative forces natur-

[1] Edmond B. Wilson, "The Cell in Development and Inheritance," second edition, p. 391.

[2] Adaptation in Pathological Processes, THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, June, 1897.

ally latent (dormant) within the cell. It will be difficult to decide in which of the two ways cell proliferation is brought about. One reason for assuming that in carcinoma of the stomach the tumor producing agency is to be sought in increase of the proliferative forces within the cell is the fact that these cells must be ground up and crushed very thoroughly before the extract will have any cancer converting effect upon experimental gastric ulcer. If the tumor producing agency were some chemical substance in the environment of the cell, we should not expect that thorough crushing and grinding were necessary to extract it, but that it could be dissolved out by repeated percolation and irrigation. However, this is an unreliable test, as the tissues must be torn up into small pieces in both instances, even if only to permit percolation. The fact that it is possible to extract a tumor producing agency from gastric carcinoma by crushing pieces of it in normal salt solution would not permit us to decide whether the tumor producing substance was derived from within or without the cell.

The modern view that cancer metastases can be effected by the transportation of single carcinoma cells is a support of the contention that the tumor producing agency is resident within the structure of the cell. In a recent investigation on the fate of dislodged and embolized tissue particles in the animal body, Paul Lengermann comes to the conclusion that the power of producing metastases is dependent upon an increase in the proliferative energies inherent in the cell, and not upon a reduction of normal tissue resistance to growth.[1]

Speaking of the influence of cell nutrition and the maintenance and undisturbed progress of cell function, Ludolf Krehl[2] says: "Nobody will expect that a tissue can maintain form and size without sufficient supply of potential energy; but the incentive does not come from the blood, as was formerly believed, but always from the parenchyma itself."[3]

Influence of Physical Laws on Cell Growth. Oscar Hertwig investigated the influence of temperature on the recently fertilized ova of rana fusca and rana esculenta, and found that certain well-recognizable stages ("Stadien") in the development of these eggs were reached quicker as the temperature of the breeding medium was increased.[4] He found that the same relation existed between rate of growth and temperature as was known to exist between reaction time and temperature.

Cell volume, within certain limits, is dependent upon osmotic pressure.

[1] "Schicksale verlagerter u. embolisierter Gewebsteile im thierischen Körper," p. 69, in "Arbeiten a. d. Pathol.-Anat. Abtheilung d. kgl. Hyg. Institut." Posen, 1901, s. 299, O. Lubarsch.

[2] Patholog. Physiologie, second edition, p. 532.

[3] "Nicht von aussen zugeführte Kräfte bringen das Heil, sondern die Zelleschaft es sich selbst."

[4] Archiv. f. mik. Anat. u. Entwicklungsgesch, 1898, 52, 319.

Cells can be made to undergo apparent growth by placing them in solutions the osmotic pressure of which is below the pressure within the cell protoplasm. In this case the cell volume increases by the diffusion of water into the protoplasm. Loeb[1] cut off the polypi from colonies of tubularia, and brought the stems in sea water of various concentrations and dilutions. He found that polypi again grew out of the stumps as long as the sea water was not concentrated to more than 70 per cent. of its volume or not diluted more than to 225 per cent. of its original volume with water; but the regeneration occurred prompter and quicker in the diluted than in the concentrated sea water. Loeb's experiments show conclusively that moderate dilution of the external medium in which a cell is bathed favors growth—*i. e.*, the solution outside must be a hypotonic one. Two other essential physical conditions to growth are (1) a certain turgescence (turgor) within the cell, and (2) expansibility of the enclosing protoplasmic envelope.

It is conceivable that cell protoplasm will become more expansible and looser by the reception of water from the hypotonic environment and a certain turgescence—that is, a hypertonic state within the cell metabolism, and the consequent increase of osmotic energy connected therewith. Increase of turgidity is always seen in rapidly growing parts. Turgidity means osmotic entrance of water into the growing cell. Claude Bernard[2] found that blood flowing through a secreting gland had lost water, and Ranke found that blood that had streamed through a working muscle had lost water.[3] To complete the logic of these instructive observations, Loeb demonstrated that the water thus lost was taken up into the substance of the working muscle; for when the muscle while at rest and before work was placed in a solution which was isotonic with the protoplasmic contents of the muscle cell, it increased in weight during its work[4]—that is, the augmentation of metabolism during work had evidently increased the osmotic pressure within the muscle cell, and the ensuing difference in pressure had induced the growth.

These observations are important for the interpretation of my own studies demonstrating the contraction of fresh cancer cells in solutions made isotonic with the human plasma, or in blood plasma itself, as if they were in a hypertonic solution—a phenomenon not observed when normal cells of the same tissue from which the cancer was taken are placed in the identical plasma or solution. It will hardly be necessary for me to emphasize that any and every growth of and in cancer cells cannot be attributed to the taking in of water only, nor can a muscle hypertrophy due to work be attributed to the taking in of water exclu-

[1] Organbildung und Wachstum, Würzburg, 1892.
[2] Phénomènes de la vie, 2d edit., 1., 169.
[3] Tetanus Physiologie, 1868, 89.
[4] Pflüger's Archiv., Bd. lxxi., 439.

sively. The water osmosis is only one phase of the process of growth, that phase which by effecting an increase of volume impresses us most as growth. The internal construction of the cell household, the deposition of new cytoplasm, is concealed from us.

When frog larvæ are analyzed at different stages of development for their percentage content of water and solid substance it is found that the entire growth of the first fourteen days consists in the incorporation of water. The body weight becomes ten times as great by water, and not until after this does the interior construction and the deposit of solid substances into the aqueous tissue begin. In the first two weeks of development of batrachian larvæ the percentage of water in the embryo rises from 56 per cent. to 96 per cent.,[1] thereafter it begins to sink again. In the light of our present knowledge we have a right to speak of the "osmotic pressure of the cell," for the cell protoplasm, as previously emphasized, is a liquid, a solution, or at least in a state of viscosity. The entrance of water into the cell substance is brought about primarily by metabolic changes effecting a hyperisotonic state in the cell with regard to its surrounding liquid environment. *This phenomenon of change of dimensions (contraction) of fresh carcinoma cells (gastric adenocarcinoma in normal plasma or solutions isotonic with plasma) is to me strong evidence in favor of the view that whatever other causes for the excessive growth of malignant cells there may be, certainly some of the causes are resident within the cell protoplasm itself.*

When we approach a consideration of the question of how the cell builds up protoplasm—that is, an inquiry into the methods and means by which it carries on the synthesis of its substance—we are confronted with a problem apparently presenting insurmountable difficulties, for all artificial syntheses are brought about by forces and agents which can never be conceived as participating in the processes of life. Such agents and forces are high pressure and temperature, concentrated inorganic acids, free chlorine, and galvanic currents of high tension. All of these are factors which would destroy cell life instantly.

So far we know definitely of the synthesis of albumin is only by the aid of enzymes (catalysator). For instance, the reconversion of albumoses, which have been formed in the gastro-intestinal canal into albumin, is attributed to some agent in the gastric wall.[2] When the stomach is isolated from an animal, but kept alive, at the height of digestion all albumoses disappear from it. It might be presumed that this does not indicate a synthesis, but a further breaking down of the albumoses. In that case, however, an increase in the non-precipitable nitrogenous substance should be demonstrable, which is not the case;[3]

[1] Davenport. "Rôle of Water in Growth," Proceedings of the Boston Society, 28, 73, 1897.
[2] Hofmeister. Zeitschr. f. Physiol. Chemie, 6, 69.
[3] Glässner. Beitr. z. Physiol. u. Pathol. Chemie, 1902, I., 328.

so that any other interpretation of this disappearance of albumoses, except their synthetic reconversion into albumin, appears illogical. Furthermore, Danilewsky and Sawgaloff have proven that chymosin (rennin) is capable of synthetically constructing an albumin from peptones and albumoses in an acid medium. This albuminous body, which they designated as "plastein," is soluble in weak acids and alkalies, insoluble in water, and can be precipitated by strong salt solution—undeniably a typical albumin constructed synthetically by this ferment.

It would be going too far to assume that all syntheses in the organism are enzyme syntheses, for an enzyme (catalyzer) is *incapable of producing anything that would not also be produced without it by other means.* Ostwald[1] groups all ferment or enzyme actions under the term "catalyse," by which he means the *acceleration of a slow or the retardation of a rapid chemical process through the presence of a foreign body (catalysator).*[2]

This definition gives the specific characteristic of enzyme action. An enzyme can, therefore, not carry out a process which would be impossible without it, but it can only influence the time in which a chemical process occurs, generally increasing the rate of the reaction, which would also take place, in a much slower or faster manner as the case may be, however, without it.

The facts, namely (1) that albumin can be constructed synthetically by enzymes, and (2) that enzymes act merely as accelerators or inhibitors of processes that can occur without them, coupled with the experimental results briefly narrated in the preceding (acceleration of cell proliferation by injection of a cell-free and sterile fluid), should suggest the possibility that abnormally rapid formation of protoplasm such as is observed *in the marvellous cell-proliferation of malignant tumors may in some way be associated with the action of an enzyme.* The catalytic origin of malignant neoplasms is by no means proven by these facts and considerations, but only made more probable. I have previously emphasized the important rôle which physical processes (osmosis) play in the growth of cells, so that it is not logical to attribute proliferation to enzyme action alone; but as we have seen that even this osmosis is due in part to a preceding hyperisotonic state within the cell brought about by increased metabolism, the function of a catalyzer is even here not inconceivable, but on the contrary very probable. Much remains to be proven before we are justified in making this conclusion indisputable.

Thus far attempts to isolate enzymes have failed, for what are believed to be ferments are variously considered, albuminous or proteid bodies — albumoses or peptones (Uróblewski) — or nucleoproteids

[1] Loc. cit. [2] See W. Ostwald, Ueber Katalyse, Leipzig, 1902.

(Pekelharing's conception of pepsin), in connection with which ferment actions have been observed. In brief, nothing is definitely known of the chemical nature of organic enzymes.

When it comes to the problem of isolating enzymes from protoplasm of cells we find that it presents insurmountable difficulties. It might be thought that inasmuch as enzymes are chemical substances, some of which are known to exert their characteristic action apart from the living substances to which they are usually attached, it might be possible to destroy the cell alone and extract the enzyme; but all protoplasmic poisons are also enzyme poisons (corrosive sublimate, carbon monoxide, sulphuretted hydrogen, hydrocyanic acid, nitrate of silver, formaldehyde, hydrogen peroxide). J. R. Green has emphasized that protoplasm itself has powerful fermentative activity. No matter what the exact relation is that the intracellular enzyme has to the protoplasm, whether it be conceived to be a detached protoplasm molecule or not, as long as it is considered a derivative of protoplasm it must be self-evident that protoplasm is capable of doing all those things which the enzymes can do. Newer conceptions concerning this subject attribute to protoplasm much more wonderful achievements than to the enzymes themselves. If the efforts to separate growth stimulating enzymes from cell protoplasm are at present futile, from the insurmountable chemical difficulties involved, we should realize that protoplasm itself may exert a more intense catalytic action than any enzyme derived from it. Our reflections concerning the nature of a substance which we assume to be capable of stimulating cell growth, and which is cell free and sterile, must end here for the present. We can only say that the agency is contained within the cell, but whether it be a special derivative of the cell protoplasm or the protoplasm itself, it is, in the light of our present knowledge, impossible to decide. A slight hope of advance lies in researches showing differences in the degree of temperature which the protoplasm and the ferment can stand without destruction. I have gained the impression that some ferments are much more susceptible to high temperatures than the protoplasms from which they are derived. For instance, the gastric mucosa of a dog can be heated to a temperature of 158° F. (70° C.) without absolutely destroying the tissue; but heating pepsin to this temperature for three hours will destroy its activity permanently. Similarly, when the so-called "commercial" pepsin is heated to a temperature of 55° to 60° C. in a moist condition it is destroyed (in a thoroughly dry state it may tolerate 160° for a short time). Nevertheless the chemical composition of the nucleo-albumin is still there as it was before the heating. The fermentative power has disappeared. Evidently ferments are not nucleo-albumins in the ordinary sense of the chemist, but something attached and associated with these nucleo-albumins.

CONCERNING THE STRUCTURE OF PROTOPLASM AND ITS CHEMICAL ORGANIZATION. The method that has become most common to familiarize us with the structure of living substance has been to start from histological elements visible under the microscope and to attribute certain physiological functions to them. The conceptions thus derived have not always acquired precision, and we have definite notions only concerning the coarser elements visible under the microscope, such as the nucleus, the chromosomes, etc. This method of observation has not been able to give the least explanation of the finer elements of the cells, the innumerable droplets, barely visible vacuoles and granules of the protoplasm, not to speak of that still finer subdivision of cell protoplasm which might be designated as ultra-microscopic. It is very gratifying, therefore, that biochemists have approached the subject of the construction of the living substance from the purely chemical standpoint, as, for instance, Franz Hofmeister has done (Chemische Organization der Zelle), who did not start from the visible architecture of the cell or protoplasm, but from its achievements and functions. He tried to investigate how protoplasm must be constructed in order to make these functions possible. As the functions of protoplasm are above all things chemical, he entered exclusively upon chemical considerations.

The hepatic cell furnishes us with an instructive example of how many chemical processes may go on in one and the same cell, and very probably go on simultaneously. We know definitely that the liver cell forms glycogen from sugar, and, reversely, sugar from glycogen. It forms urea from ammonia and amido acids. It decomposes hæmoglobin, and under the splitting off of iron it converts it into bilirubin. It can manufacture cholic acid from a substance still unknown, and pairs it with taurin and glycocoll. This same cell can combine phenols with sulphuric acid to form the ethereal sulphates, and it can retain or render harmless poisons that are conducted to it. Nothing is more certain than that these performances represent only a fraction of the chemical versatility of the hepatic cell, for we must certainly assume that the same cell can in addition execute other chemical processes necessary for the oxidation of the food materials brought to it for hydration and assimilation. The supposition that there is a division of labor among the liver cells, one group of cells manufacturing one product and the other another, is untenable because the hepatic cells are of the identical structure throughout the liver, and their relation to the blood, lymph, and biliary vessels so alike that an assumption of a division of labor is not justifiable. There is no escape from the conclusion that all liver cells are chemically equivalent, and each cell is capable of performing all of the described chemical processes and possibly many more. When we reflect that all this chemical activity is invisible by the microscope,

and that many chemical processes must occur side by side simultaneously, it is difficult to conceive of the construction of protoplasm that would make such a manifold and wonderful chemical activity possible.

Many years ago Hoppe-Seyler expressed the opinion that such activities in living cells as were intelligible at his period were due to enzymes, and since then it has been possible in many cases to extract such intracellular ferments from the innermost structure of the cells and to establish their significance for vital processes. When we compare the instrumentarium—chemical substances and reagents necessary for chemical transformations in the laboratory—with the processes as they occur in living protoplasm (as much as has thus far been accurately observed) we cannot fail to be impressed with the astounding simplicity and conformity to the end in view exhibited in the means which protoplasm employs to accomplish its chemical purposes. In order to induce a reaction in the laboratory we need a reagent, *i. e.*, either an alkali or an acid, or perhaps the application of heat; but the reagents which the cell employs are calculated to fill the chemist with envy.

The food substances and the oxygen and other possible stuffs which act upon each other within the cell do not, as a rule, belong to the normal cell household, but enter it from the blood. The reagents, however, which induce the reactions, must always be present, and they must in some way be protected from being washed out of their domicile by the constant flow of liquid passing through the cell. These reagents must be either soluble in water or infinitesimally divided in it. They must be capable of accomplishing relatively large chemical performances, and not be consumed or used up during their activity. Such qualities are only known to be possessed by agents which the chemist has designated as *catalyzers*. The bearers of the chemical energy in the cell are catalyzers of a colloidal consistency (Hofmeister). According to Hofmeister, we are justified in assuming that the living cell protoplasm contains all the ferments necessary to the execution of the chemical performances observed in connection with that cell. This view is supported by the knowledge obtained of the physiological chemistry of quite a number of cells in the animal body. For instance, we know that the hepatic cell can yield up (1) a proteolytic ferment, (2) a ferment that can transform combined nitrogen of amido acid into ammonia, (3) a fibrin ferment, (4) a glykase, (5) a maltase, (6) a ferment capable of splitting up nucleins, (7) a lactase, (8) an aldehydase, (9) a lipase, and (10) a ferment similar to the gastric chymosin. Here we have definitely established the presence of ten different ferments in a single hepatic cell. *In addition to this we may believe that the synthetic construction of the cell tissue itself requires a special ferment to make possible the chemical processes necessary for the upbuilding of protoplasm.* From what I have said in connection with normal and abnormal cell

growth *it is evident that it is this ferment to which must be ascribed the power of accelerating or inhibiting cell growth.* If we once accept ten different ferments which really have already been definitely established as existing in the same cell, there is no logical reason why the remaining unexplained chemical functions of the cell should not also be ascribed to peculiar ferments, and *I can conceive of no reason why cell growth itself should not be accelerated or inhibited, as the case may be, by a particular enzyme.*

A considerable number of capable modern physiologists have accepted the view that every chemical reaction in the cell has its particular catalyzer corresponding to it. It is easy to recognize that this view may lead us too far, for the specific nature of the ferments is not always such as to restrict their action on one single chemical body, but they may be able to transform a greater or lesser number of substances of similar construction (tyrosinase, for example, may oxidize a large number of aromatic substances). Furthermore, it is conceivable that very labile bodies may arise as a result of chemical transformations in the cells, which are promptly changed into other forms under the existing conditions, and, therefore, no ferment is necessary to explain such transformation. A further revelation which modern chemistry has brought particularly through the researches of Kastle and Loevenhart, to which I have already referred, is the reversibility of the action of ferments. Should this power of reversibility of enzyme action be confirmed with other ferments, it opens up the possibility that many analyses and syntheses are brought about by the same ferment according to the existing requirements and chemical conditions in the cell.

It is probable that the chemical organization of the cell is capable of reckoning with all possibilities, whether they occur within or without the cell, whether they are an advantage or hostile to the cell state. There are no reliable reasons for believing that the organic antitoxins, coagulins, and antihæmolysins owe their origin to definite catalytic cell agents which are equipped for the production of such protective substances. M. Jacoby holds that the antibodies do not act like ferments. The cell is even equipped with ferments for the purpose of committing suicide or digesting itself when it has arrived at a state or condition in which it is no longer of use to the cell state. This phenomenon of cellular autodigestion has recently been observed in tissues which have been perfectly protected from the invasion of microorganisms.

Cellular autodigestion has been studied in all animal organs and occurs in all except those that show a very slight degree of metabolism. M. Jacoby gives to this phenomenon the designation autolysis. It is well known that the various forms of lymphoid cells contain an abundance of a trypsinoid ferment, and it is possible that autodigestion

occurs by virtue of such an enzyme. Petrey[1] found that in neoplasms autolysis was much more intense than in normal corresponding tissue. The proteid substances and the nucleins of the cell, the glycogen and the fat, are split up similarly as they would be in the intestines, and a number of diffusible substances result, such as sugar, leucin, tyrosin, fatty acids, etc. This is a form of catalytic colliquidation occurring in single cells, or in cell complexes which have passed the stage of their usefulness; and if this process occurs in an otherwise normal organism there is no reason why the end-products of such cellular autodigestion should not be taken up by the blood and lymph and be absorbed and assimilated to the advantage of the general organism just as they would be if they had been absorbed from the digestive tract.

An astounding fact which has been revealed by modern investigation in connection with this phenomenon is that bactericidal substances are set free during autolysis. It is well known that proteolytic digesting mixtures are first-class culture media for bacteria. For this reason the production of bactericidal substances during cellular autodigestion demands admiration.

If I have in the preceding suggested the probability of the action of intracellular catalytic agents in accelerating or inhibiting cell growth, I do not wish to be understood as meaning that these agents are the only factors which determine the growth and the character of the cell protoplasm. What I have said concerning the rôle of osmosis will prevent my being misunderstood in this connection. An intracellular enzyme cannot construct protoplasm out of itself—it can only build it up out of the materials furnished to it; and as these materials must vary with every species and even with every individual, it is probable that the elements of which protoplasm is constructed within the cell must be presented in a certain definite form, in order that a normal cell protoblast shall result. This is an important point, for it explains how variations in the chemical composition of the cell juices (dyscrasias) may be determining factors for the character of the resulting cell structure.

The simultaneous action of so many intracellular ferments within the same cell sometimes representing diagonally opposite processes, such as oxidation and reduction, hydration and the withdrawal of water, is only conceivable if we accept, with Professor Edmund B. Wilson, the foam structure of protoplasm, that is the view which assumes that protoplasm is held within a foam-like structure of countless ultra-microscopic compartments, retorts, or vacuoles. We must assume also that the walls of these ultra-microscopic spaces are not affected by the reaction which takes place within them. For instance, that the walls of the

[1] Hofmeister's Beitr. z. chem. Phys. u. Path., 1902, ii.

compartment or vacuole in which oxidation takes place are resistant to the oxidase, and that the walls of the space in which proteolysis takes place are resistant to the proteolytic enzyme. Such a possibility is, so far as our present knowledge goes, only conceivable within the living cell by means of its catalytic agents, which may decompose an albuminoid body of one composition completely and yet leave another very similar albuminoid body entirely intact. For instance, the proteolytic ferment of the liver can completely decompose the globulin of the hepatic substance, but it does not attack another albuminous body of similar composition with which it may even be in contact. The intactness of this so-called foam structure of protoplasm is, therefore, an essential condition for the normal action of the intracellular enzyme. A destruction of these ultra-microscopic partitions may lead to serious consequences, and it is here that the importance of what Welch calls the "more subtle and partial damage of cytoplasm and nucleus" exercises its detrimental influence in destroying the normal intracellular architecture and making possible the liberation of ferments and disturbing the normal chemical equilibrium.

We must conceive of the normal and orderly performance of the cell as brought about by the aid of an admirable and highly sensitive system, embracing among other things a transference and transformation of chemical, electrical (ions) and other specific forms of energy, and of accelerating and inhibiting enzymatic (catalytic) agents; of the latter a great variety, each acting in its own ultra-microscopic compartment. We must conceive of a delicate mutual adjustment and conformation to purpose among the many little laboratories within the cell household. And even these conceptions are coarse and inadequate if we knew in reality of the incomprehensible fineness and perfection of intracellular chemical activity. But it will be readily understood that very slight damage to cytoplasm in the sense of Welch[1] will be sufficient to destroy this beautiful arrangement, and enzymes which are useful lambs in the orderly household may become destructive lions when the partitions are broken down.

In the preceding I hope to have made possible the conception that abnormal cell growth may be due to something else than bacteria At the same time I do not wish to deny the possibility of a deleterious influence exerted by bacteria and favoring the development of malignant neoplasms. Malignant neoplasms represent a great group of abnormalities, and I agree with Hansemann that there cannot be a uniform cause for all these manifold types of abnormal cell growth. But if I admit the possibility of bacteria as active in their etiology, it is only as indirect agents in causing these more subtle and partial damages, to cyto-

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, June, 1879, p. 19.

plasm, which liberate ferments on the one hand, and destroy them on the other; for we must not lose sight of the possibility that even within the cell abnormal growth may be due to excessive action of one ferment stimulating growth, or to the absence of an enzyme necessary to inhibit it.

Reversibility of Enzymes. Basing our views on the chemical mechanism of growth on the phenomenon of the reversibility of enzymes, it is intelligible how increase in the dimensions and weight of the cell mass may be brought about by two different and divergent processes. There may be only the synthetic enzyme concerned in the control of growth, or there may be a second intracellular enzyme that inhibits growth, by analysis of protoplasm already formed. Under the conception of enzyme reversibility, however, it is not necessary to assume the existence of two distinct enzymes—one synthetic, the other analytic—for reversibility means that one and the same enzyme may exert diagonally opposite chemical effects if need be. The synthetic enzyme may act like a governor upon the metabolic machine of the cell. If the influx of utilizable substances is normal or subnormal it works synthetically and builds up protoplasm; if the influx is too great it reverses this state of affairs and breaks down protoplasm analytically. We are already very close to the view of the self-regulation of metabolism by reversible enzymes in the case of the liver glycogen, and of fat digestion and absorption. A simpler conception of glycogen metabolism cannot be held than that controlled by an enzyme which converts sugar into glycogen, when there is an excessive ingress of sugar, but reversely converts glycogen into sugar when there is an insufficient influx of sugar.

The metabolism of fat would be readily intelligible if we similarly accept the existence of an enzyme in the fat cells which would be capable by means of its reversibility of maintaining a definite equilibrium between the soaps in the blood and the fats in the fat cells, or which some enzyme (to apply the protothesis to fat digestion) were capable of splitting up fat into fatty acids and soaps within the intestinal lumen, and after their absorption recombining them into neutral fats again.

The doctrine of an intracellular enzyme being active during normal cell growth brings with it the suggestion of a detriment to this enzyme when we are confronted with abnormal cell growth. No doubt the intracellular laboratories are seriously upset, and the anarchistic growth may be due to several possible factors:

1. The self-regulating catalytic mechanism of the synthetic enzyme may be destroyed; it can only build up, no longer decompose.

2. There may have preceded a lesion to the finer structure of the cell substance, a lesion though delicate, yet irreparable, paralyzing the self-regulating catalytic metabolism.

3. The normal tissue tension in the environment of the degenerate

cell can hold it in check for a while if the lesion has struck only one or a few cells—the cell state is threatened by the leaven of rebellion, but perhaps the normal tissue equilibrium of the cell state may be restored if the anarchy has not struck too many cells; they may be forced to autodigestion, or some other form of disintegration, and for all that we know this may occur often if the cell state is vigorous and the metabolism normal.

4. But if the protoplasm apparatus of a considerable complex of cells is disturbed simultaneously, the normal cells in the environment, the tissue juices, etc., are helpless to overcome the excessive growth.

Some have argued that cancers always grow from out of themselves ("aus sicht selbst"—Ribbert); that is, one cancer cell always grows from a preceding cancer cell—until the original degenerate cell is reached. But I can conceive of no reason why the altered metabolism of large groups of malignant cells should not be able to produce such detriment, by chemically affecting adjacent normal cells, that their cytoplasm also receives a subtle damage, sufficient to paralyze the self-regulatory catalytic apparatus for growth (a kind of enzymatic, not bacterial infection). This extension of catalytic infection to other cells, even to the cells of the bloodvessels, is, of course, as yet an assumption; but it is well known that all the various tissues in an autonomous (Lubarsch) neoplasm are in a state of abnormal proliferation, particularly the bloodvessels which give evidence of a peculiar development (Klebs),[1] explainable only on the assumption that this tissue also has been drawn into the cell anarchy, but not to the same extent and character as the cells of the neoplastic parenchyma.

The cell has within its protoplasm certain recognizable structures which may be termed the organs of the cell, viz., the nucleus and its constituents, the chromatophores, centrosomes, the plastids—the passive bodies (E. B. Wilson), the metaplasm or paraplasm, the vacuoles, with their inclusions and secretions, the pigments in certain locations; all of these things signify that the cycloplasmic meshwork is not everywhere in the cell of the same chemical composition or reactive energy. This is already suggested by the fact that widely different reactions, sometimes chemically opposed to each other, occur in the same cell simultaneously. In the cytoplasm, synthetic and analytic transformations occur, not always by the same chemical reactions, but by a series of widely differing reactions. The decomposition of glycocoll to form urea, for example, is not conceivable without a liberation of the NH_2 group from a part of the glycocoll molecule, then follows an oxidation of the remainder, and eventually a combination of the fractional parts. But it is essential that these reactions should occur in well-ordered sequence, other-

[1] Pathologie, Bd. xi.

wise urea cannot be formed in this way. A lawful and ordered sequence of this and numerous similar composite reactions within the cell necessitate the conception that the different agents work separately in different compartments of the cell, we are forced to accept a chemical organization which excludes the idea that the cytoplasm is everywhere the same chemically—*in short, there cannot be an ubiquitous chemical equivalence of protoplasm.* The colloidal reagents then are separated by walls, to them impenetrable and secure from their chemical influence. Let us conceive of a lesion, invisible to the microscope but destroying these partitions, and we can realize the danger of liberation of enzymes; they can now attack all elements formerly inaccessible, or they may even attack each other.

This is the proper place to be reminded of the many theories of the causation of cancer, attributing it to some form of irritation (to which the parasitic theory may be classed also) or to trauma.[1]

METASTASES.—Virchow has expressed the opinion that malignant tumors may extend in three different manners:[2] First, by immediate propagation—that is, by direct extension or growing over from one organ into another; second, by dissemination—that is, detachment of tumor particles which settle down in another position; for instance, if a carcinoma of the stomach extends through or perforates into the peritoneum, the cells of the carcinoma may gravitate to any portion of the peritoneum and cause independent secondary growths. The third manner of extension is highly interesting from the standpoint illuminated in the preceding pages, and in order not to express the views of this great master in a wrong manner I will quote his own words: "This manner of metastatic extension makes it very probable that the transference occurs by means of liquids, and that these possess the power to create an infection ('Ansteckung'), which causes the individual parts

[1] Hemmeter. Cancer Etiology, Diseases of the Intestines, vol. i. p. 677.

It may be objected that I am here moving on very hypothetical ground, and having in the beginning of this article doubted the value of hypotheses, that I am myself now adding assumptions which go beyond the demonstrable state of facts concerning cell growth. But I must contend that I am not formulating a new hypothesis when I assume that all cell growth must be under the control of an intracellular catalyzer; I am simply for the time being using an assumption based on present observations, which, however, have not yet been sufficiently comprehensive. We know of the causal relation between cell growth, cell chemistry, and catalyzers. Certain reactions occur in the cell, certain products are built up, certain substances decomposed. We can isolate the synthetical and analytical products; we have in many instances isolated the enzymes and repeated their characteristic reactions in the test tube. We know from the nature of certain intracellular reactions that they must inevitably occur in separate compartments. Hence we are forced to believe that the growth of the cell structure itself is a separate and distinct performance, that there must be self-regulating cytoplastic syntheses in the cell, and that in pathological cell growth this chemical process is deranged. I am here making temporary use of a "protothesis" (see W. Ostwald, Naturphilosophie, s. 399), with the view that further researches may instruct us whether the assumption is correct or not. The difference between a protothesis and a "hypothesis" is that the former adds nothing to existing observations which cannot further be tested. A protothesis is a temporary conclusion drawn from experience, observation, or experiment, for the purpose of subjecting it to critical testing concerning the limit of its value and significance.

[2] Cellular Pathologie, s. 258.

to form a reproduction of the same mass which was originally present." Is it not possible that Virchow here conceived of a form of catalytic action? The other two forms of metastatic extension can, of course, not be denied. The third type, however, has been emphatically denied, and has not as yet been recognized by any pathologist of prominence.

It was Waldeyer[1] who first demonstrated by systematic investigation that carcinomas grow into the lymph spaces and vessels, and so may reach the general circulation. This observation has been abundantly confirmed; and, furthermore, the characteristic difference has been established that carcinomas readily grow into the lymph vessels, but that the bloodvessels offer them considerable resistance. (It is claimed by Hansemann that sarcomas, on the other hand, may readily break into the bloodvessels.) A number of prominent special investigators of this subject have called attention to the comparative rarity with which metastases occur by the way of the circulation, and Hansemann[2] suggests that a large part of the detached carcinoma cells are destroyed in the blood circulation.

It is essential to distinguish between the local factors which can be recognized as active in the development of a primary tumor and the general factors which determine its future fate, particularly the development of metastases. Of the local factors the most prominent ones have already been sufficiently considered, but the factors which control the formation of metastases are very manifold; and in this connection I should like to call attention to the following: (*a*) Condition of other organs; (*b*) abnormal states of the entire body, the simultaneous action or refusal to act of the regulatory apparatus of the organism; (*c*) acquired or inherited disposition, spoken of as individual disposition (the carcinoma dyscrasia). It is in this connection that the collective investigation of the German government, under the direction of Prof. E. von Leyden, gives promise of throwing light upon the cancer etiology as far as it is associated with bodily constitution, vocation, inheritance, nutrition, manner of living, etc.

In this connection I desire to call attention to a possible explanation of the rarity of metastatic extension of cancers by way of the blood circulation. The idea was suggested by the investigations of Belfante, Carbon, J. B. Bordet, Ehrlich, and Morgenroth, previously referred to. Concerning the hæmolytic action of the serum of one animal upon the erythrocytes of an animal of another species, it is necessary that the effect of the serum of normal individuals upon isolated cancer cells of other individuals should be studied, for it is conceivable that the cancer cells represent forms of protoplasm which have become *so far alienated and emancipated from the general physiological laws of the body that they*

[1] Virchow's Archiv., 1867, Bd. xli.

[2] Loc. cit., p. 91.

actually represent cells foreign to the body against which the serum brings into action its means of defence just as it would against any other foreign intruder. This is, to my mind, a very hopeful direction for investigation, with a view to prospective prophylaxis or treatment. The point of inquiry will have to be: *"Does not the organism contain in its blood serum defensive substances capable of destroying cancer cells as long as they are not flooding the circulation in excessive quantities? and, if so, how can this natural means of defence be augmented?"* The fact that carcinomas extend preferably by the way of the lymph vessels is highly suggestive of the means of defence in the blood circulation above referred to.

CRITICAL RETROSPECT. In the preceding I have attempted to consider the pathogenesis of cancer from the standpoint of the chemist and physiologist rather than from the bacteriological standpoint. The principal hypotheses were referred to and the difficulties in the way of the acceptance of the parasitic theory briefly given. The changes which cells may undergo under normal and abnormal conditions were presented in the paragraph on "metaplasia." In order to narrow down the point of inquiry the investigations were made upon one type of carcinoma only—that with which the author has greatest familiarity—the adenocarcinoma of the stomach. A *résumé* of recent experiments on tumor transplantation preceded the writer's personal experiments, the main conclusion of which was that gastric ulcers can be experimentally produced, and that the edges of these gastric ulcers can be brought to undergo adenomatous transformation by the injection of a cell-free and sterile fluid obtained from a cancer of the same organ from the same species of animal.

Inasmuch as this filtrate was destroyed after being heated to 60° C., it was concluded that the agent active in causing this abnormal proliferation at the edges of experimental gastric ulcers was a catalytic agent. It might be objected here that the successful experiments were too small in number to permit of reliable conclusions. On this point I wish to state that the experiments extended through years, and at times had to be given up entirely for five to six months for lack of material, because I believed that I could work only with cancer material developed spontaneously in animals, and that cancers even if produced experimentally in the method described did not contain the catalytic agent in sufficient quantity to cause adenomatous proliferation in other animals. The main reason for this is to be sought in the fact that the experimental adenomata are very small; in three out of four cases their recognition depended upon microscopic examination. Although I was and still am in communication with the principal veterinary schools of this country, and even with Professor Ostertag and Professor Regenhogen, of the "Thierärtzliche Hochschule," of Berlin, I have come into the possession of only one dog with cancer of the stomach. The investigations would

have been indefinitely delayed had I depended exclusively upon this material. At present I am still engaged with these experiments, and by the aid of Profs. Frank Martin and J. Mason Hundley, whose aseptic technique I hope will secure me a larger number of recoveries from the operations described, I hope to be able to report an additional number of successful experiments in the near future.

The fact that in one instance adenomatous degeneration identical with ulcus carcinomatosum developed at the edges of a pre-existing gastric ulcer spontaneously gives promise of a new source from which to derive canine cancer material. At the same time this spontaneous development of cancer may be interpreted as a criticism of my deductions. It may be argued that the injection of the sterile and cell-free cancer extract does not prove that an enzymatic agent is necessary to start already proliferating cells into a condition of malignancy, for this instance proves that they may pass over into that state without any extraneous agency. Upon closer consideration, however, this criticism can hardly be considered as invalidating the main deductions, for throughout our considerations I have not argued that something entirely extraneous to the cell is needed to cause cancerous proliferation, but; on the contrary, I have tried to emphasize that the agent is something which the cell contains or produces within itself, but its regulatory mechanism is destroyed, etc.

The adherents of the parasitic theory might argue that the cancer extract, though sterile, may contain the products of bacterial metabolism, toxins, etc., which are soluble and can pass through a Pasteur filter, and that it is these toxins which acted as the agency causing the abnormal growth. This objection it is impossible to meet. It might be urged, however, as far as we can judge from the infectious diseases, that bacterial toxins may after injection cause the clinical picture of the disease, but not the characteristic histological alterations in the cells of the tissue which are concomitant with an infection by the living bacteria. Injections of tuberculin, for instance, cannot cause tubercles.

A possible objection is also found in the fact that adenomas of the digestive canal have been caused by mechanical injuries; for instance, by cutting off the lower ends of the glands of Brunner and of Lieberkühn. This observation has not as yet been satisfactorily investigated, and it has not been claimed that adenomas caused in this way were malignant. Lubarsch[1] succeeded in producing a fibro-adenoma in the liver by transplanting a portion of liver into an artificial lesion made in another region of this organ. He does not maintain, however, that this was a malignant—or, as he prefers to designate it, an "autonomous"—neoplasm, and presumes[2] that his experimental neoplasm would have eventually given way to a connective tissue cicatrix.

[1] Zur Lehre v. d. Geschwülsten, etc., loc. cit., p. 253. [2] Loc. cit., p. 254.

In the preceding it has been pointed out that the autonomous development of neoplasms (adenomas) may be due to subtle damage to cytoplasm, which is in fact another way of expressing the traumatic and irritation etiology of neoplasms. I do not wish to dispute such possibilities. On the contrary they are to a large extent necessary for the bringing about of deranged catalytic action already described. It is important to emphasize in this connection that I have not succeeded in producing an adenocarcinoma by cutting or bruising the gastric glands, not even when they were in the environment of a pre-existing lesion.

The studies concerning the effect of osmotic pressures upon normal and cancer cells suggest the influence of physical energies upon normal as well as abnormal cell growth, and that future investigations along this line even promise to throw light upon this problem.

The immediate and specific causes of cell division are next considered. The theories of Virchow, Thiersch, Boll, and Weigert are abstracted, and the conclusion reached that the stimulus to normal cell growth is of a chemical nature.

The influence of physical laws upon cell growth constitutes another paragraph, which is followed by a consideration of the question of how the cell builds up protoplasm, that is, the methods and means by which it carries on the synthesis of its own substance. It is here suggested that this is effected by means of intracellular catalyzers.

The conception of how the cell protoplasm must be constructed, its possible chemical organization, concludes with a support of the view accepting the foam structure of protoplasm, and of a special catalyzer regulating the synthetic construction of protoplasm.

As the cell is conceived to be made up of innumerable ultra-microscopic compartments, the more subtle and partial damage of cytoplasm and nucleus in disordering the orderly and normal performances of intracellular catalysis are next set forth.

The reversibility of enzymes is then briefly considered, and the possibility of a damage to the ferment which controls the upbuilding of protoplasm is suggested, and also that there cannot be ubiquitous chemical equivalence of protoplasm.

In the final paragraph on metastases the suggestion is thrown out that possibly the blood serum contains defensive substances effective in the destruction of cancer cells, and the study of this means of defence gives hope of a more successful form of treatment.

In speaking of the transformation which the edges of the experimental ulcer in dogs underwent after injecting the sterile extract of canine gastric adenocarcinoma I may have unwittingly designated them as "gastric adenocarcinomas." What I really mean throughout the article is not that a genuine gastric carcinoma had been produced in my experiments, but that such a histological transformation was effected that the

microscopic appearance resembled that of a beginning adenocarcinoma. This expression is as far as the experiments justify me to go. I do not wish to imply that a typical cancer had been produced in this way, for this designation brings with it numerous attributes which it was impossible to bring into the experimental results. Above all things, I am not able to say whether the cell proliferation thus produced experimentally would have gone on to develop a genuine malignant tumor had the animals been permitted to live, or whether the proliferation would have been arrested and its place taken by a cicatrix. To complete the conception of carcinoma we must demand the evidences of malignancy, as is expressed in the production of metastases. Metastases were not produced in any of the animals examined. They occurred only in the dog in which a gastric ulcer had developed spontaneously.

RUBBER TISSUE AS A DRESSING.

By G. Tucker Smith, M.D.,
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In treating any lesion of the skin in which an ointment is indicated as a dressing, it is of prime importance that the parts should, first, be thoroughly protected from infection from without; second, the ointment used should be kept in constant touch with the parts; third, the dressings, when changed, should come away without sticking and without damaging the new-formed and delicate epithelium, and, fourth, that the dressing should be kept on as long as possible. All these requirements are admirably filled by rubber tissue. The parts having been cleansed with warm sterile water and green soap, should then be dried. The ointment is next spread on and covered over smoothly with sterile rubber tissue. Sterile lint is next applied and the whole secured with gauze bandage. Several cases are cited to illustrate its benefits:

F. J. McA., warrant machinist, U. S. N., aged thirty-three years, native of Brooklyn, N. Y., was, on November 24, 1902, while at work repairing a steam launch, severely scalded by escaping steam on both feet and wrists. The pain was severe, but was relieved by wet picric acid dressings and a hypodermic injection of morphine sulphate, one-quarter grain. The next morning it was found, on removing the dressings, that large blisters had formed. These were punctured, and the serum evacuated with aseptic precautions. A 10 per cent. boric ointment was then applied to the affected parts, and over this rubber

tissue, lint, and a bandage. The dressings were changed from time to time without adhering to the skin or causing pain. By December 3d he was well, the old skin having been entirely replaced by the new without infection.

Mrs. F. B., a young married woman, came under my charge last summer. She was suffering with a severe case of psoriasis. The disease had existed for almost two years, and had been very rebellious to the usual treatment of chrysarobin and collodion, locally, with arsenic internally. The eruption was confluent and covered the arms, forearms, the lower part of the body, the lower extremities, and the scalp. A 10 per cent. ointment of chrysarobin was applied to the arms and forearms with the rubber tissue daily. The improvement was prompt and gratifying. She had made for the body a jacket lined with the tissue. She moved to another locality early in October, but kept up the treatment faithfully. I heard from her from time to time that the eruption was gradually but steadily disappearing, and in January she wrote me that it had entirely gone, with the exception of a few small spots.

B. S., an infant, aged eight months, was recently treated by me for acute eczema of the scalp. The little fellow was suffering greatly from the itching and consequent loss of sleep. Rubber tissue was sewed into a tight-fitting hood of light cotton material. Zinc ointment (ʒss–ℨj) was applied, and the hood tied on closely and kept on day and night. The scalp was cleaned daily with sweet oil and the ointment and hood re-applied. The relief was evident, and in five days the eruption had disappeared.

In conclusion, I would state that doubtless this method has been used by others. As far as I am concerned it is original. I do not believe, however, that its advantages are generally known, and hence deem it worthy of report.

REVIEWS.

HANDBUCH DER PATHOGENEN MIKROÖRGANISMS.

HANDBOOK OF PATHOGENIC MICROÖRGANISMS. Edited by PROFS. W. KOLLE and A. WASSERMANN, with the collaboration of PROFS. BUCHNER, CORNET, EHRLICH, ARMAUER, HANSEN, KITT, H. KOSSEL, METSCHNIKOFF, A. NEISSER, NOCARD, WEICHSELBAUM, and others. Jena: Gustav Fischer, 1902.

FROM its great extent, its voluminous and widely scattered literature, and the increasing variety and novelty of many of its subdivisions, bacteriology is eminently fitted for encyclopædic treatment. Many books have been planned to this end, and some of them have been highly successful, but it is inevitable that a single volume cannot contain many details that even the general reader may wish to know. A more serious result in such books depends on the fact that the most indefatigable writer cannot keep up with all departments of the subject and give the essential part, well-digested, to the reader. The undertaking of Kolle and Wassermann seems well adapted to meet the need, both in size and plan, and in the collaboration of a large number of authors, all of whom are well known as investigators and writers, and many as discoverers or specialists of the first rank. The work is devoted especially to the micro-organisms important in pathology, including that of the lower animals. (Facts of general interest regarding saprophytic parasites are, however, considered in the chapter on General Morphology and Biology.) Methods of diagnosis and clinical and epidemiological data are to be thoroughly discussed, and a whole volume (the third) is to be devoted to the important subject of immunity. The whole is to appear in seventeen rapidly following fasciculi, with a quarto atlas in six fasciculi. The first instalments of text and atlas are most promising. Beginning with a brief but comprehensive general view of the historical development of "Infection, Immunity, and Prophylaxis," by R. Abel, "General Morphology and Biology" are taken up by E. Gotschlich. All the details of the subjects are discussed with great thoroughness, and, as is so useful in such a work, with references by number to original sources in connection with each statement, every section having a classified bibliography at the end. The second chapter is not finished in the one hundred and fifty pages it takes up in the first fasciculus. Each part is treated with admirable fulness. The sections on "Latent Infection," "Auto-infection," "Excretion of Infectious Organisms from the Body," and "The Sources of Infection" may be particularly mentioned as valuable alike to the general medical reader and the specialist, but the more recondite topics, such as metabolism of bacteria, enzymes and ferments and variability are equally well done. Dogmatism is safely avoided, and conflicting views, inevitable in the present

state of our knowledge, are fairly stated, though the author does not hesitate to give his own opinion. The text is illustrated with figures in black and colors. The *Atlas* is to be made up of photographs, partly from negatives by Prof. E. Zettnow, partly from those furnished by the several authors. The first fasciculus contains a short description of the technique by Zettnow, and two plates, with thirty-eight pictures, illustrating the morphology of various species, chiefly bacteria, with a uniform amplification of one thousand diameters. Though the pictures have not the artistic beauty of photogravures, they are all the better for the purposes of study and comparison. Altogether, the work promises to be a satisfactory as well as an indispensable one, useful to the student and the physician, as well as the professional bacteriologist and teacher. We note, with satisfaction, that investigations made outside of Germany are often referred to, and, as the parts treated in the first instalment deal with topics that have not been studied as much in America as have many others, there is every reason for believing that the numerous researches of American bacteriologists will be more adequately referred to than hitherto. The mechanical execution of the book shows the skill and care we have become accustomed to in the publications of Mr. Gustav Fischer. The price, about twenty dollars (single copies are not to be sold), is relatively low, and should assist in a wide distribution of the Handbook. G. D.

THE INTERNATIONAL TEXT-BOOK OF SURGERY, BY AMERICAN AND BRITISH AUTHORS. Edited by J. COLLINS WARREN, M.D., LL.D., Hon. R.F.C.S. Eng.; Professor of Surgery in Harvard Medical School; Surgeon to the Massachusetts General Hospital; and A. PEARCE GOULD, M.S., F.R.C.S., Surgeon to Middlesex Hospital; Lecturer on Surgery, Middlesex Hospital Medical School, etc. Second edition, thoroughly revised. In two volumes. Vol. I., General and Operative Surgery; Vol. II., Regional Surgery. Philadelphia and London: W. B. Saunders & Co., 1902.

THE exhaustion of the first edition of this work within two years speaks for its reception by the profession and by the medical schools. The changes and additions noticeable in this second edition are to be found particularly in the chapters dealing with military and naval surgery, the lymphatic system, and the spleen. Changes and improvements are also observable in the discussion of the surgery of the kidney. The work consists of two volumes, each containing about 900 pages. It is the labor of about sixty authors, English and American, all well known and eminently fitted to write the portions assigned them.

The first volume is devoted to general surgery and the second to special surgery. The various chapters are not signed by their respective writers, but a list of the chapters and their respective authors is to be found in the front of each volume. We feel that it would be an additional advantage to have the name of the writer appear at the head or at the end of each chapter, so that, without trouble, the reader could learn who wrote the portion of the book which he is consulting. The illustrations are particularly to be commended, not that they are exceedingly numerous, but because they are particularly good. There are nine full-page illustrations in colors. In the first volume we find but

few points for criticism, and many for commendation. The chapter on Fractures is the most generally acceptable brief treatise on fractures with which we are acquainted. We are glad to see an author who is willing to urge a departure from the old lines of treatment, which consisted in prolonged fixation and a postponement of any motion of the part for a number of weeks, and to substitute for these a more limited time of immobilization, followed by early movement and early massage. For fractures of the lower end of the humerus involving the joint, he advises only acute flexion, and in this we thoroughly concur. If his suggestions regarding the treatment of fractures at the lower end of the radius were followed there would be fewer cases of stiff wrists and finger joints following these injuries. In the treatment of fractures of the patella, too, particularly by the open method, it is shown that the old treatment of nearly interminable fixation is to be abandoned. We regret that the writer of the chapter on Injuries of the Joints has failed to make any mention of compression in the treatment of sprains, particularly of the ankle-joints, since we feel that no chapter on this subject can be complete without recommending this method of treatment, and more particularly that mode of compression known as the Gibney adhesive strip dressing. Dislocation of the hip-joint and diseases of this joint are given extensive consideration.

The chapter on the Heart and Bloodvessels is an excellent one, and the author's attitude toward the treatment of injuries of the heart appeals to us as essentially the right one, urging as he does, prompt surgical intervention in all cases of punctured wounds of the heart and pericardium.

The second volume, which deals with regional surgery, deserves a hearty commendation. Each subject is dealt with in a thorough manner by an author who has devoted much time and special attention to its study. It is this fact which makes us feel that the book is more valuable than one written by a single authority. The illustrations are in most respects new, and not the ones we are accustomed to meet with in every surgical work. One of the closing chapters of this volume deals with traumatic neuroses. This is a subject well included in a surgical work of this kind.

In closing we can say that we believe this work to be more generally satisfactory than any book of similar proportions. The second volume is especially valuable because of the excellent selection and assignment of authors. J. H. G.

GENERAL PARESIS, PRACTICAL AND CLINICAL. By ROBERT HOWLAND CHASE, A.M., M.D., Physician-in-Chief, Friends' Asylum for the Insane; late Resident Physician, State Hospital, Norristown, Pa.; member of the American Medico-Psychological Association; Fellow of the College of Physicians, Philadelphia. Philadelphia: P. Blakiston's Son & Co., 1902.

DR. CHASE has had a long and rich experience in studying and treating the insane, and it goes without saying that a book of his must be good. The expressed purpose of the book is to be a guide to the general practitioner, the man into whose hands the victim of paresis falls long before he is seen by the specialist, the man who alone has an opportunity to help him. It is vitally important that the family doctor should know

and thoroughly know the symptomatology of paresis, for on its early diagnosis hangs the possibility of amelioration. Dr. Chase gives a very good account of the disease. His work is almost wholly clinical. He dwells but little on morbid anatomy. In the clinical histories he uses no cases of his own, but quotes from the literature. The reason for this is manifestly a kind desire not to run the risk of hurting the feelings of relatives of his patients. The effect may be, however, to make some readers who are unacquainted with him think that he is one of those youngsters just out of college who, seized with the ambition to be great, make a book with the scissors. We need not say this is not a scissors book. The data are from the world at large; the opinions are from Dr. Chase, and are based on his knowledge and his experience. Physicians in general practice look askance at books on special subjects. They expect to find a strange vocabulary and obscure discussions on subjects either obscure in themselves or made so by the writers. They sometimes find what they expect. In Dr. Chase's book they will find a clear and simple account of general paresis. They will also learn what can and cannot be done by treatment. These things are worth knowing.

C. W. B.

DISEASES OF THE STOMACH: THEIR PATHOLOGY, DIAGNOSIS, AND TREATMENT, WITH SECTIONS ON ANATOMY, PHYSIOLOGY, CHEMICAL AND MICROSCOPIC EXAMINATION OF STOMACH CONTENTS, DIETETICS, SURGERY OF THE STOMACH, etc. Pp. 894. By JOHN C. HEMMETER, M.D., Ph.D., with many original illustrations and a lithograph frontispiece. Third enlarged and revised edition. Philadelphia: P. Blakiston's Son & Co., 1902.

DR. HEMMETER is to be congratulated upon maintaining the high standard of excellence manifested in the first edition of this attractive volume, the most important and comprehensive treatise on the subject in the English language. The general scheme of the work is that indicated by the sub-title, and each section, whether devoted to the anatomy and physiology of the stomach, to analysis of the stomach contents, to the diagnosis and medical treatment of the various gastric ailments, to the diet kitchen, or to the surgery of the stomach, is attractively developed and brought up to date. It is the author's plan to present an elaborate treatise, whence appears a good deal which would be superfluous in a less pretentious volume devoted rather to an exposition of personal experience and a presentation of the gist of the subject than to a detail, as is here done, of not only what is essential in apparatus and of approved value in treatment, but what may be of little utility to either the specialist or to the general practitioner. Here the subject is intended to be presented in what may be called encyclopædic form, and this detail seems rational if, at times, it may be vexatious to the reader.

The volume is increased by nearly one hundred pages over that of the first edition. This last received an extensive review in these columns, and the faults there noted, inseparable from the primary production of such a work, have practically all been eliminated. We may say that in glancing over the work we see little to condemn and much to praise.

It must be said it is regrettable that Dr. Hemmeter cannot offer a more certain remedy than ergot for the control of "copious and persistent" hemorrhage occurring in gastric ulcer, and that, indeed, in this particular he still pins his faith to this drug, even though its use has, as he remarks, the indorsement of Riegel, Ewald, and Nothnagel. As the reviewer has insisted upon in several publications (see, especially, *System of Practical Therapeutics*, vol. ii., p. 949, Lea Bros., 1892) in the past ten or more years, ergot is contraindicated rather than of value in hemorrhage from ulcer requiring active treatment, that of copious extent and often of persistent form, then due commonly to arterial erosion and not to capillary oozing. In frank hemorrhage thus occurring, ergot, from its well-known power of causing constriction of the arterioles and not of the larger vessels, thus raising resistance *a fronte*, is likely, if it has any effect at all, to augment the bleeding. The reviewer has never observed any benefit from the use of ergot in hemorrhage of this character. We think Dr. Hemmeter might well have mentioned the utility of calcium chloride by enema or by hypodermoclysis and of gelatin similarly used in recurrent hemorrhage. It is on one or both of these agents rather than on ergot that the physician must rely.

It is a pleasure to note Dr. Hemmeter's view as to the status of the abused employment of electricity in diseases of the stomach. The results of Hemmeter's experiments are in line with Meltzer's and others, that the gastric muscularis is unresponsive to direct faradic and galvanic stimulation as it is therapeutically employed in diseases of the stomach. These laboratory experiments are supported by past extensive use of this remedy by the writer. Beginning its employment in 1890, through the teaching of Einhorn, after some years' thorough trial of electricity in all classes of cases in which it seemed theoretically indicated, the reviewer's final judgment was that its utility is narrow, and, though he still employs it discriminately, he does not use it with the notion of influencing gastric motility through direct effect on the stomach muscles. He has never been able to satisfy himself that by either galvanism or faradism could the capacity of an anatomically-dilated stomach be reduced. It is not long since that a still verdant, though active, laborer in the field of "gastro-enterology," in an article on the subject, related cases in which but an application or two of intragastric electricity had a noteworthy effect (susceptible of demonstration) in diminishing the capacity of a dilated stomach and raising its inferior curvature.

We are not altogether in agreement with Dr. Hemmeter as to the utility of HCl employed as he recommends it for its digestive effects in cases of absence of the gastric secretory function—achylia gastrica. The amount of HCl required for proteolysis, discussed by Dr. Hemmeter in another section of the work, would indicate the inefficiency of the dose suggested in achylia—one drachm of the dilute acid in divided portions after meals. This dose, though efficient in cases of mere subacidity, can be of no practical utility with complete absence of gastric secretion. One drachm of the dilute acid is approximately equivalent to 190 c.c. of 0.2 per cent. HCl, and this is far and away inefficient for satisfactory saturation of the proteids of an ordinary meal. As calculated by Blum and confirmed by Chittenden and others, including the reviewer, with a daily consumption of 100 grammes of dry proteid, some 4500 c.c. of 0.2 per cent. HCl is required, and with this there would be no excess appreciable of free acid. With the employment of HCl, as a digestant

in achylia, pepsin must, of course, be coincidently administered, unless it is merely desired to form acid albumin. The writer, after extensive trials of HCl, both to promote a return of its own secretion and as a digestant, in a series of carefully studied cases of achylia, some years ago abandoned its use as impracticable other than when employed as a stomachic. It is in cases of achylia gastrica that real digestive effects are obtained from an active preparation of papain or of the pancreas. Fresh pineapple juice, mentioned by Hemmeter, although of similar value, is less practicable for continuous administration. In at least two of the reviewer's cases he noted decided interference with the digestive function of the stomach under the HCl therapy. In each case chymifaction was apparently accomplished through the conservative regurgitation of intestinal (pancreatic) juice into the stomach. HCl may, however, be employed as a stomachic or as a stimulant to the return of its own secretion (in nervous anacidity), administered either alone or in combination with vegetable bitters, but then is most efficient given on the empty stomach; then only can sufficient be administered, except after a very moderate meal, to exert an antiseptic effect.

In conclusion, we again congratulate Dr. Hemmeter on his excellent treatise, which we unhesitatingly recommend to those interested in the subject. D. D. S.

STUDIES OF THE INTERNAL ANATOMY OF THE FACE. By M. H. CRYER, M.D., Professor of Oral Surgery, Department of Dentistry of the University of Pennsylvania. Philadelphia: The S. S. White Dental Mfg. Co., 1901.

THIS book might well be called an atlas of the anatomy of the bones of the face, accompanied by a running comment on the general principles of their pathology and surgery. Probably the same modesty which induced the author to give his work such an unostentatious title has likewise led him to condense the really wonderful amount of valuable information which it contains within such a limited number of pages. The value of a monograph of this character cannot be estimated by its size. In Dr. Cryer's book there is not a paragraph which could be omitted without the loss of something of distinct value to teachers and students of the anatomy of the head. Of the illustrations, every one of them is original in this work, and too much cannot be said in their praise. They are pictures of specimens, and, having been made by the author himself, they show the points which he really wished to elucidate. In the course of his work Dr. Cryer has discovered many new and important points in the osteology of these bones, particularly as regards the course of the various nerves which are found pursuing their way through so many of them. Many instances might be brought forward to show in what way the heretofore received ideas as to the regional anatomy of the face are disturbed by Dr. Cryer. For instance, we would direct particular attention to his studies of anatomy of the inferior dental and the infraorbital nerves. This important monograph of Dr. Cryer's should be in the hands not only of every student of anatomy, but of every dental surgeon and rhinologist. Its practical value can hardly be over-estimated. F. R. P.

CLINICAL PSYCHIATRY. A TEXT-BOOK FOR STUDENTS AND PHYSICIANS. Abstracted and adapted from the sixth German edition of Kraepelin's *Lehrbuch der Psychiatrie.* By A. ROSS DEFENDORF, M.D., Lecturer on Psychiatry in Yale University. The Macmillan Company, 1902.

THE purpose of this book is twofold—to make the views of Kraepelin more accessible to American readers and to provide a concise text-book. The author has succeeded. The book opens with a section on general symptomatology, after which the various forms of mental disease are studied in order. There is a short account of idiocy and imbecility at the end. The article most interesting to us is the one on dementia precox. Cretinism, even in an American book, deserves more than two pages. There is a short bibliography at the end of each subject, in which only important papers are mentioned—a bibliography for use and not to impress the reader with the author's erudition. The descriptions of disease are clear, the English concise and not verbose, and there is an absence of non-understandable words sometimes met with in books. Dr. Defendorf makes no attempt at classification; he has no chapter on that subject and he deserves thanks therefore. In the present state of knowledge no consistent classification of mental diseases is possible, and an inconsistent classification is useless. Altogether the book is admirable, and we advise every student, undergraduate or graduate, to study it.

C. W. B.

MEDICAL MICROSCOPY: DESIGNED FOR STUDENTS IN LABORATORY WORK AND FOR PRACTITIONERS. By T. E. OERTEL, M.D. 8vo., 362 pp., with 131 illustrations, some of which are colored. Philadelphia: P. Blakiston's Son & Co., 1902.

THIS little book is a straightforward presentation of the branches of medical science for which a knowledge of the microscope and its teachings is essential. It makes no claim at fulness or authority, and is designed for the practitioner and the student who are deprived of the advantages of laboratory training. When it is seen that a description of "The Microscope," "Fixation of Tissues," "Bacteria," "The Blood," "Urine," and the various fluids of the body are covered in the headings, one is rather amazed that the author has made a book that is so readable and accurate within its limitations. We are a bit skeptical as to the necessity for such a treatise on the ground of "a little knowledge;" but, granted the necessity, the accomplishment is more than creditable. The illustrations are good and help the text.

F. P. G.

A MANUAL OF GENITO-URINARY AND VENEREAL DISEASES. FOR THE USE OF STUDENTS AND PRACTITIONERS. By LOUIS E. SCHMIDT, M.D., of the Chicago Polyclinic. In one handy 12mo. volume of 250 pages, with 21 illustrations. Philadelphia and New York: Lea Bros. & Co., 1902.

THIS little volume, one of the medical epitome series, aims, in the words of the author, "to afford a comprehensive survey within a com-

pact space." Although, as a rule, we question the utility of such works to the practitioner who is really in search of information, this epitome is exceptional in the amount of really valuable material which it offers. It is to the medical student, however, who seeks to attain the most information in the briefest possible time, that the present book will prove especially useful as an aid in the lecture-room and a supplement to larger works. As far as consistent with the small space devoted to the subject, the treatment of the various genito-urinary and venereal affections is fully given and is thoroughly up to date. H. M. C.

THE AMERICAN YEAR BOOK OF MEDICINE AND SURGERY FOR 1903: A Yearly Digest of Scientific Progress and Authoritative Opinions in All Branches of Medicine and Surgery. Arranged with critical editorial comments by eminent American specialists, under the editorial charge of GEORGE M. GOULD, A.M., M.D. In two volumes. Volume I., General Medicine, fully illustrated. Volume II., General Surgery, fully illustrated. Philadelphia, New York, London: W. B. Saunders & Co., 1903.

THE *American Year Book* is once more before us, and fully maintains the high standard of excellence which has given it its reputation in previous years. It is impossible in a work of this character to pick out any particular department for special notice, as the various sub-editors, under the able supervision of Dr. George M. Gould, have all of them performed their work in so uniformly excellent a manner that the choice of any one of them for particular commendation would be invidious. During the temporary lapse of the *Index Medicus* books of this character have been compelled to serve in its place, but even with the reincarnation of that invaluable periodical such a work as the *Year Book* will continue to remain an indispensable adjunct to the library of every scientific man, because in no other way can he attempt to familiarize himself to any extent with the current medical literature. F. R. P.

PROGRESSIVE MEDICINE. A Quarterly Digest of Advances, Discoveries, and Improvements in the Medical and Surgical Sciences. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia; Physician to the Jefferson Medical College Hospital; Laureate of the Royal Academy of Medicine in Belgium, of the Medical Society of London, etc. Assisted by H. R. M. LANDIS, M.D., Assistant Physician to the Out-Patient Medical Department of the Jefferson Medical College Hospital. Volume IV., December, 1902. Philadelphia and New York: Lea Brothers & Co., 1902.

THE December volume of *Progressive Medicine* contains the recent literature on the Diseases of the Digestive Tract and Allied Organs, arranged by Einhorn; Anæsthetics, Fractures, Dislocations, etc., by Bloodgood; Genito-urinary Diseases, by Belfield; Diseases of the Kidneys, by Brad-

ford; Physiology, by Brubaker; Hygiene, by Harrington; and Practical Therapeutic Referendum, by Thornton. It is useless to say anything regarding the style and standing of *Progressive Medicine*. It has already won for itself an enviable place in medical literature.

The volume before us contains liberal abstracts on the subjects under discussion and excellent critical remarks by the various editors. The first portion of the book, although prepared by a medical man, will be found of particular interest to surgeons as well as to physicians, since it deals with the various pathological lesions of the whole alimentary canal, in the treatment of which the surgeon and physician are so frequently associated. The use of the œsophagoscope, for instance, is explained and illustrated. Diverticula and dilatations of the œsophagus are also discussed. Recent literature on hour-glass stomach, perforation of the stomach, and appendicitis is also dealt with in this portion of the volume. The literature on hemorrhage, surgical shock, and fractures is particularly well presented.

It is impossible to refer to all the various chapters, but it can be said that this volume is in keeping with the standard of its predecessors, and will be found of great value to anyone wishing to acquaint himself with the latest literature on the subjects here presented. J. H. G.

CLINICAL METHODS: A GUIDE TO THE PRACTICAL STUDY OF MEDICINE. By ROBERT HUTCHISON and HARRY RAINY. Fifth edition. Chicago: W. T. Keener & Co., 1902.

BESIDES being a repository of clinical laboratory methods and of the numerous instruments of precision, familiarity with which is now required of every student, the book is really an excellent and trustworthy manual of physical diagnosis. That portion of the book, in fact, comprising about one-third, distinguishes it very favorably from many more pretentious works on the same subject. Precision of statement and lucidity of style—indispensable conditions of a successful didactic work—are conspicuous features, while a judicious selection of diagrams illustrating physical signs and the logical classification of phenomena add to its practical usefulness. The index also deserves a word of commendation. Theoretical discussion and interpretation of phenomena are purposely reduced to a minimum, but perhaps a little more liberality in this respect would have proved acceptable to the reader; instead, the pruning-knife might have been applied a little more vigorously in the choice of clinical instruments from among the great number that compel selection. Some of these might well be spared in a practical manual for students; we refer particularly to blood pressure instruments, the uncritical presentation of which must prove misleading to anyone who has not had personal experience with these devices. In spite of the authors' disclaimer of any attempt at completeness in the list of laboratory methods included in the volume, the latter will be found to contain all those that are essential and practical, and leave a margin for personal preference. Four editions have been exhausted since the first appearance of the book five years ago, and we sincerely hope the success of the fifth will be equal to that of its predecessors. R. M. G.

LES DIFFORMITÉS ACQUISES DE L'APPAREIL LOCOMOTEUR PENDANT L'ENFANCE ET DE L'ADOLESENCE. Par le DR. E. KIRMISSON, Professeur de clinique chirurgicale infantile à la Faculté de médecine, Chirurgien de la hôpital Trousseau, Member de la Société de Chirurgie, Membre correspondent l'American Orthopedic Association. Avec 430 Figures dans le Texte. Paris: Masson et Cie, 1902.

A PRIMARY anatomical scheme of classification, with subdivision of chapters from the pathological viewpoint, is that used in most works of orthopedic surgery. The treatise of Young was the first, in our knowledge, to depart from this precedent. Its primary divisions are partly devoted to lesions of the individual tissues and partly to an etiological and pathological classification of the subject.

It is from the latter and more scientific standpoint, that of the etiologist and pathologist, that Kirmisson has divided the 645 octavo pages of the volume under review into four books, entitled as follows: I. Tuberculosis. II. Rickets and Sequent Troubles of Development during Infancy and Youth. III. Deformities Sequent to Affections of the Nervous System. IV. Deformities of Traumatic and Inflammatory Origin. These books are subdivided into chapters with anatomical headings. It is interesting to note that the author has placed the greater part of his remarks upon scoliosis in the book devoted to rickets.

Excellent and profuse pen-and-ink drawings, some radiographs, and a few half-tones admirably illustrate not only the pathology of the lesions described, but also most serviceable mechanical aids in the accurate record and successful treatment of acquired deformities. The author is to be no less congratulated on the wide scope of this volume, written from the limits of personal experience than on the practicality and cosmopolitan character of the appliances he commends. The book is notably free from the elaborately impossible contrivances that often astonish the American reader of German works on surgical topics. The paper and typography are all that could be desired. The binding is of paper, and as is unfortunately the rule with French books, an alphabetical index is omitted.

To the student, the general surgeon, and to the orthopedist especially, this should prove a most serviceable volume. J. M. S.

LECTURES ON CHEMICAL PATHOLOGY IN ITS RELATION TO PRACTICAL MEDICINE. Delivered at the University and Bellevue Medical School, New York City. By C. A. HERTER, M.D., Professor of Pathological Chemistry, University and Bellevue Medical School, New York. New York and Philadelphia: Lea Brothers & Co., 1902.

DURING the last few years modern methods of scientific study have thrown the most astonishing light upon certain chemical changes which take place in the body cells both in health and disease—changes which are quite as important as the pure morphological alterations of the cells. Certain phases of pathology and chemistry have thus come to overlap, and in consequence there result the problems of chemical pathology. Dr. Herter's book cannot be too highly praised. The subject, intensely interesting in itself, derives a double value from the

manner in which it is presented, and although dealing principally with experimental medicine, forms a sound basis for the application of certain principles to practical medicine. The volume is divided into thirteen lectures. The first, which forms rather an introduction to the general subject, treats of the chemical defences of the body against diseases, and includes a short review of the bacteriolytic actions of the body fluids as well as the manner in which the body cells contrive to rid the body of chemical toxins. Then follow four lectures on the chief food-stuffs and their fate in health and disease, while two more lectures are devoted to a discussion of excessive fermentation and putrefaction in the digestive tract, and one each to the chemical pathology of gastric and intestinal digestion. The tenth and eleventh chapters deal with the chemical pathology of hepatic diseases, and the twelfth, a most important one, with diabetes. The book ends with a discussion of starvation, under-nutrition, and obesity. Each subject is gradually expanded and developed, so that the more complicated processes are introduced by the simpler ones, and thereby become clear and are easily understood. When theories are advanced they are based upon sound experimental evidence, and the latest researches which have any bearing upon the subject are freely made use of. Indeed, much of the subject-matter can be found in no other text-books, and is compiled from very recent original literature. One of the many excellent features of the book is the short bibliography appended to each lecture, in which are given a few of the most important references on the subject under discussion. The book is well written, and the valuable material which it contains is read with pleasure. W. T. L.

A Text-book of Materia Medica, Therapeutics, and Pharmacology. By George F. Butler, Ph.G., M.D., Professor of Materia Medica and Therapeutics in the College of Physicians and Surgeons, Chicago, Medical Department of the University of Illinois, etc. Fourth edition, thoroughly revised. Philadelphia and London: W. B. Saunders & Co., 1902.

It is with much satisfaction that we take up this edition of Butler. It appeals to the student because it is systematic and thorough, and to the physician in that it contains in readily accessible form a large amount of material. The present edition differs from its predecessors in showing considerable rewriting, more confidence in some therapeutic measures—perhaps the result of more extended experience—and a longer list of remedies. In particular the results of laboratory work have been fully utilized to amplify the matter contained in "Physiological Action," and the journals devoted to therapeutics—of ever-increasing value and possibly number—have been drawn upon to fill out "Therapeutics." And in the process some ancient statements from hereditary text-books have lapsed into deserved oblivion. Thus the fourth edition comes much nearer to our ideal than did the first, six years ago. This volume should be held in high regard if for no other reason than that it lays so much stress on the untoward as distinct from the poisonous action of drugs, and the tables, pp. 48 to 53 inclusive, as well as the

preliminary statements, are too important to the practitioner to be passed without comment. Of information in which many text-books are still deficient, organotherapy and serum therapy may be cited as satisfactory in quantity and value of statements contained. The question of the day, "The Relation of Physical Chemistry to Pharmacology and Therapeutics," has been intrusted to Dr. Martin H. Fisher, who has developed it in a little over eight pages. As a well-arranged, classified, and comprehensive treatise on materia medica and therapeutics and some cognate subjects of importance to students, written in a clear and convincing style, we commend this as we have the other editions. The many items in which we noted improvements over its predecessors verify the claim of its thorough revision, and in this the valuable assistance of Dr. Smith Ely Jelliffe is acknowledged by the author. We congratulate the author on the realization of his desire to make the fourth in every way worthy of the success of the earlier editions.

R. W. W.

PHYSICAL DIAGNOSIS: DISEASES OF THE THORACIC AND ABDOMINAL ORGANS. By EGBERT LE FEVRE. Philadelphia and New York: Lea Brothers & Co., 1902.

A BOOK, we think, of permanent utility to the student and practitioner of medicine has appeared in Le Fevre's *Physical Diagnosis*. It is one of the best works of its size upon this subject we have as yet seen.

Recognizing the necessity of a thorough understanding of those factors to which the production of physical signs are due, in order that the facts elicited may be properly interpreted, the author has spared no pains in showing their basis and underlying principles, and has illustrated the subject with numerous original cuts and photographs. In addition to the usual subjects treated of in the text-books of this character, there is appended a chapter on Examination by Means of the X-ray, a method of diagnosis which has proved of such substantial value in many otherwise obscure conditions that the subject can no longer be ignored in up-to-date medical books.

Considering that the work is in its first edition there are but few typographical errors, and while exception might be taken to some statements made in it, yet on the whole the volume may be heartily indorsed as a valuable addition to the library of the practitioner or student.

G. W. N.

SAUNDERS' QUESTION COMPENDS, No. 25. ESSENTIALS OF HISTOLOGY. By LOUIS LEROY, B.S., M.D., Professor of Histology and Pathology in Vanderbilt University, Medical and Dental Departments, etc. Second edition, revised and enlarged. Pp. 263, with 92 illustrations. Philadelphia and London: Wm. B. Saunders & Co., 1902.

A SECOND edition within a short period would indicate that this book meets and supplies a demand. The text is a concise and in the main accurate epitome of the subject, yet not so concise as to lose in clear-

ness. The new photomicrographs are a valuable addition to the book, and it is to be hoped that they will stimulate the author, in the event of further editions, to replace or improve the original sketches which appear crude in contrast. F. P. G.

A TEXT-BOOK OF ANATOMY, BY AMERICAN AUTHORS. Edited by FREDERIC HENRY GERRISH, M.D., Professor of Anatomy in the Medical School of Maine, Bowdoin College. Second edition, revised and enlarged. Philadelphia and New York: Lea Brothers & Co., 1902.

THE first edition of this work won for it a place among the very best of our general descriptive anatomies. This second edition shows a number of improvements over the first, particularly the chapter on osteology, to which has been added a number of excellent colored drawings, and the six contributors are to be congratulated on this excellent volume. One fact strikes the reader throughout, and that is that the book is written to teach. It is not composed of a mass of dry facts monotonously set forth, but the subjects are each made as interesting and comprehensive as possible. An excellent introductory chapter of twenty pages by Gerrish gives the student an idea of what anatomy is, and how it should be studied. Every student should read repeatedly the author's instructions regarding the method of study. It is this which is most essential, and which is most usually wanting in medical students. Another feature of this book which appeals strongly to us is the great number of excellent illustrations. What the student needs in studying anatomy in the absence of the cadaver is pictures and diagrams, which help him to comprehend and remember what he reads. In this respect we feel that the work before us surpasses any other with which we are acquainted.

The nervous system, always a difficult subject for the student, is set forth in the clearest and simplest manner, and beautifully and thoroughly illustrated. One of the closing chapters deals with relational anatomy, and is illustrated by a number of cross-sections of different portions of the body and photographs showing surface markings. At the end of the volume, also, are to be found a dozen skiagraphs showing the normal osseous system.

In his preface the editor thanks his publishers for their "remarkable liberality" in the matter of illustrations. Certainly they have been liberal; but, as we have said before, this matter is such an important one in a book of this nature that we feel the publishers have shown discretion as well as liberality.

In closing this review we feel that we can recommend this text-book of anatomy by American authors as probably the most generally satisfactory book of its kind and size published in recent years. J. H. G.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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An Epidemic of Paratyphoid Fever. De Feyfer and Kayser (*Münchener medicinische Wochenschrift*, 1902, vol. xlix. pp. 1692, 1752) report a carefully studied epidemic of paratyphoid fever occurring in the practice of the former, at Eiberg, in Holland. The epidemic consisted of fourteen cases, one of which was apparently a mixed infection with typhoid fever. The cases were characterized by a short prodromal stage of one to four days, with irregular elevations of temperature, loss of appetite, and pain in the head, back, and legs. The course was favorable in all cases, and there were no very serious sequelæ. The acutely infectious nature of the malady was undoubted. The temperature curve was typical in the mild as well as in the severer cases. There was a remittent and intermittent period. In the remittent period, both morning and evening exacerbations were occasionally to be made out. Sometimes the fever fell critically. The case of mixed infection with typhoid had an afebrile course. The pulse in general bore a direct relation to the height of the temperature. With regard to the intestinal tract, there were at the beginning of some cases vomiting and borborygmi; the tongue was almost always more or less coated; there were abdominal pains, though there was no tenderness on pressure. An ileocæcal murmur was always to be made out. The spleen was, as a rule, not palpable, but enlargement was to be made out by percussion. There was almost always diarrhœa, followed sometimes by constipation. The stools were thin, yellowish, and foul-smelling. The urine was, for the most part, free from albumin. In all cases examined for that purpose there was a diazo reaction and increased quantity of indican. The sensorium was generally clear, though the patients were sometimes somnolent and apathetic. A roseola was made out in half of the cases. The blood serum of the patients in all cases agglutinated paratyphoid bacilli of the type β of Schottmüller. Bronchitis was a common

complication. Angina was often observed at the beginning of the disease. In a few instances there was slight intestinal hemorrhage.

The authors review the work of Schottmüller, Kurth, and Brion, and Kayser, who have distinguished two types of paratyphoid bacilli, the second type, the organisms of which were agglutinated by the serum of these cases, being far the commonest.

Blood cultures were negative, possibly because but small quantities of blood were taken. The authors point out the fact that paratyphoids are not so remarkably rare, having been found in 6.6 per cent. of 180 cases of what was clinical typhoid fever by Schottmüller and Kurth.

The cases reported by de Feyfer constituted a definite endemic, resembling in all respects a mild typhoid fever. Such cases must be distinguished (1) from typhoid fever; (2) from the typhoid form of influenza; (3) from gastro-intestinal catarrh, with or without fever. The similarity with typhoid fever is so great that "the differential diagnosis as to whether typhoid or paratyphoid is present is impossible on the basis of clinical observation alone." The agglutinative reaction settles the question. There was reason to believe from the observation of this epidemic that the water from the River Berkel was, in some instances, the source of infection.

The authors conclude that "we have in paratyphoid fever evidently a widespread typhoid-like acute infectious disease which may, under similar etiological conditions, occur as does typhoid fever under the form of an epidemic.

"The cases so far observed have had a favorable course.

"Paratyphoid fever must, in our opinion, be treated from a hygienic-sanitary standpoint just as typhoid fever; that is, it is in the interests of public health to insist that the cases be reported and subjected to the same rules of disinfection as in typhoid fever.

"The diagnosis of paratyphoid is to be made by the help of the agglutination test or by cultivation of the bacteria."

On the Circulatory Disturbances in Collapse in Acute Infectious Diseases.—PASSLER and ROLLY (*Münchener medicinische Wochenschrift*, 1902, vol. xlix. p. 1737), from Curschmann's clinic, contribute some extremely interesting observations upon the physiology of the circulatory disturbances occurring in collapse in acute diseases. The object of their investigation was to clear up the question, so important from a therapeutical standpoint, as to whether the circulatory collapse occurring under these conditions is due to cardiac weakness or to vasomotor paralysis, or to both. Von Stejskal and Waller estimated the functional capacity of the heart by comparing the carotid pressure with that in the left auricle. If the fall in carotid pressure be due to vasomotor paralysis rather than to weakness of the heart itself, the auricular pressure will also fall, while on the other hand, if the arterial pressure falls on account of the cardiac weakness, the auricular pressure will rise. Pässler and Rolly found that by extirpating the splanchnic nerve on both sides in rabbits a practically complete vasomotor paralysis follows, though, as a rule, the carotid pressure falls more than the auricular pressure, indicating that the heart works under somewhat more unfavorable conditions than ordinarily. If in such a case, however, abdominal massage be carried

out, or compression be made upon the aorta above the diaphragm, it is found that the heart is abundantly capable of carrying out the extra work put upon it. Such a heart, however, after a relatively short period of time, becomes gradually insufficient. That this insufficiency is probably due in great part to the deficient nourishment of the heart wall, due to the vasomotor paralysis, was shown by the fact that by large injections of salt solution into the jugular vein the carotid pressure was materially raised, while the action of the heart improved so that in some instances there was an actual increase of power above that previously following compression of the aorta. The authors believe that they have a measure of the functional power of the heart in the quotient between the auricular and carotid pressures when increased demands are brought upon the organ, as for instance, by abdominal massage or aortic compression. These methods the authors have utilized to determine whether the fall of blood pressure coming on at the height of diphtheria and pneumonia depends upon cardiac weakness or upon vasomotor paralysis. In experiments upon animals poisoned with diphtheria toxin they were able to show that the collapse depended always upon a diminution in the response of the vasomotors to sensory stimulation, while by the employment of aortic compression or abdominal massage the power of the heart was found to be rather increased than diminished. In some cases in which the reflex excitability of the vasomotors was entirely lost, the functional capability of the heart was found to be actually accentuated. Only gradually, at varying periods of time after this, did evidences of actual cardiac weakness develop. In the same manner as after splanchnic extirpation, the power of the heart even under these conditions might be sustained for a considerable length of time by very large infusions of sodium chloride. Similar conditions were observed in pneumococcus infections.

Portions of their conclusions are worthy of quotation. "The circulatory disturbances which occur at the height of various acute infectious diseases depend upon a paralysis of the vasomotors. The heart plays no part in the production of the fall of blood pressure occurring in the collapse. Increased work on the part of the heart may retard the dangerous fall of the arterial pressure for a time. When, finally, the blood pressure falls, the heart is secondarily damaged."

The authors, however, find evidence that the diphtheritic poison does exercise a direct influence on the heart muscle, though a similar condition was not to be made out in pneumonia. "It is not impossible that this diminution in the power of resistance of the diphtheria heart favors and hastens the oncome of secondary heart weakness in vasomotor paralysis. The heart in diphtheria, however, does not contribute toward the development of the circulatory disturbance which comes on at the height of the infection."

[The possible clinical importance of these interesting observations is evident. Such studies as these emphasize the necessity of more systematic and accurate records of the variations in blood pressure in acute febrile diseases than have been heretofore customary in most clinics.—W. S. T.]

The Nature of Non-tropical Chyluria.—FRANZ and VON STEJSKAL (*Ztschr. f. Heilkunde*, 1902, Band xxiii. (N. F. Bd. iii.), Heft 11, Abth. F., Heft 4, p. 441) contribute a valuable inquiry into the nature of the chyluria

of temperate climates. After a careful study of forty-one cases of non-tropical chyluria, all that they have been able to collect from the literature, to which they add a minutely studied case of their own, and a discussion of the theories heretofore advanced to account for this condition, they reach conclusions some of which are worthy of reproduction.

European chyluria forms, as does the tropical variety, a perfectly sharp disease picture not to be confounded with other affections. Of the two conditions brought forward as different characteristics, namely, the presence of parasites in the urine, as well as the appearance of hæmaturia in tropical chyluria, their absence in European chyluria, the first alone actually exists, the presence of parasites. The second point is not sufficiently important to be of weight in suggesting a difference in the cause of the two affections, especially inasmuch as the authors find that in the European form of the disease blood corpuscles have been made out microscopically in all cases, while in one the admixture of blood was evident macroscopically.

The similarity of the changes in the urine in both forms of the disease speaks in favor of a like cause. Their own observations in one case of European chyluria show absolutely no differences from the conditions found in the more common tropical form. These observations the authors believe to have resulted in a demonstration of the following facts:

"(1) The dependence of the chylous change in the urine upon the introduction of fat into the intestinal canal, proven
  (*a*) by the disappearance of the fat in the urine under starvation;
  (*b*) by the appearance of fat-free urine under a diet very poor in fat;
  (*c*) by the excretion of specific fats, such as olive oil colored with Sudan red, erucin, lipanin, by the urine following their introduction into the gastro intestinal tract;
  (*d*) by the circumstance that fat which is with difficulty absorbed appears in the measure of its absorbability.
(2) The lack of relation between the excretion of fat in the urine and its introduction by other methods, as, for instance, by subcutaneous introduction of colored fat.
(3) The early appearance of alimentary glycosuria, caused, probably, by the increased quantity of sugar in the chyle, resulting from the great amount in the intestinal canal.
(4) The appearance of chiefly mononuclear leucocytes in the chylous urine."

Their observations lead them to believe that the chylous character of the urine is to be regarded as the result of an actual mixture of chyle with the urine, and they point out the fact that in two instances of European chyluria a lymphatic obstruction was made out. The autopsy in Ponfick's case shows that a dilatation of the thoracic duct and of the intra-abdominal lymph vessels may, even in the absence of parasites, be associated with a chylous condition of the urine, the obstruction to the flow of lymph resulting eventually in the entrance of chyle into the lymphatics of the kidney or other parts of the uropoietic system.

They conclude that both European and tropical chyluria are the result of passive congestion of the chyle passages with consequent entrance of chyle into the uropoietic system.

SURGERY.

UNDER THE CHARGE OF

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An Operation for the Radical Cure of Aneurism Based upon Arteriorrhaphy.—MATAS (*Annals of Surgery*, February, 1903) states that in the operation that he has proposed the sac is, as a rule, not extirpated nor disturbed, except in so much as is required to evacuate its contents and freely expose its interior, and in this way it may be regarded as a derivative of the old Antyllian operation. Apart from this it differs essentially from either of the classical procedures in the fact that no ligatures are applied to the main artery, and that the circulation in the sac is arrested and hæmostasis is secured solely by suturing the arterial orifices found in the interior of the sac. Again, in suitable cases—that is, in the true sacciform aneurisms with a single orifice of communication with the parent artery—this method will allow the operator to obliterate the aneurism without obstructing the lumen of the artery or interfering with the circulation in the injured or diseased vessel, a great desideratum which should never be lost sight of when operating upon this class of cases. Finally, it differs essentially from the Antyllyian operation in the fact that the cavity of the sac is not simply packed or drained and left to heal by granulation, but is at once obliterated by inverting or infolding the walls of the sac with the attached overlying skin. The flaps thus formed are sutured to the bottom of the cavity, so that no dead spaces are left to suppurate or favor secondary complications. This operation is applicable to all aneurisms in which there is a distinct sac and in which the cardiac end of the main artery can be provisionally controlled. It is especially applicable to all forms of peripheral aneurisms of the larger arterial trunks, and, while the author has had no experience with similar lesions of the large visceral trunks, the principle suggested would appear to be applicable to abdominal, aortic, and other accessible forms of abdominal aneurisms. It is particularly indicated in the treatment of traumatic aneurisms in which the wounded artery communicates with a well-developed and circumscribed sac, and in all fusiform and sacculated aneurisms, whether traumatic or idiopathic, in which the conditions for securing provisional hæmostasis can be obtained. The method proposed does not contemplate the treatment of arteriovenous aneurism and the circumscribed or diffuse pulsating hæmatomas of recent origin which result from arterial and arteriovenous injuries. These cases offer admirable opportunities for the conservative application of arteriorrhaphy, with the view of preserving the lumen of the injured vessels and thus maintaining their functional value as blood carriers.

The steps of the operation as applied to peripheral aneurisms of the larger arteries are: (1) Prophylactic hæmostasis; (2) incision of the skin and exposure of the sac; (3) opening of the sac and evacuation of its contents, recognition of the type of sac, number of openings, etc.; (4) closure of the aneurismal orifice by chromicized catgut sutures; (5) removal of constrictor and test of sutures; (6) obliteration of the aneurismal sac.

The author has operated with success upon four cases by this method, two of which were direct traumatic aneurism of the brachial, caused by gunshot wounds, one of which involved the lower and the other the upper third of this artery, one femoral and one popliteal, and both of the so-called spontaneous variety. In conclusion the author submits the following propositions: (1) That the recognized advantages of the radical operation for the cure of aneurisms of the peripheral arteries, as demonstrated by the statistics of the last decade, can be greatly increased and the sphere of application of this operation can be broadened by the adoption of the method of suture and obliteration of the sac instead of the classical ligation of the arteries with or without extirpation, as hitherto practised. (2) That the closure of the arterial orifices which supply the aneurismal sac, whether these be single or multiple, by means of suture and within the aneurismal sac itself, greatly simplifies the technique of the radical operation, and is a reliable means of securing hæmostasis. (3) That in favorable cases—and the sacular aneurisms with a single orifice communicating with the lumen of the larger arterial trunks are the most favorable—it is possible by careful suture to obliterate the aneurismal opening without obstructing the lumen of the parent artery, thus protecting the limb from the risk of gangrene. (4) It is also possible in favorable cases of fusiform aneurisms of traumatic origin, and in those in which the sac material is healthy and pliable, to restore the lost continuity of the artery by building a new channel which will connect the two main orifices of communication and restore the interrupted circulation in the parent vessel. This result can be obtained by utilizing the sac in the manner previously described by the author. (5) That the fear that atheroma and other degenerative changes will interfere with the healing and repair of the arterial tunics has been greatly exaggerated is shown by the abundant experience of the aseptic period in the ligature of sclerotic arteries in continuity, in the absence of secondary hemorrhage in the amputated stumps of the aged, diabetic, and other arterially diseased subjects (Heidenhain, Webber, Barwell and others), and is still demonstrated more fully by the observations and statistics of the partisans of the radical operations by extirpation (Delbet, Kubler, Ransohoff, Annandale and others), who have reported numerous successful results in spontaneous as well as in traumatic aneurisms. (6) The fallacy and dangers of the old operation of Antyllus lie (*a*) in the fact that he preliminary ligation of the main artery above and below the sac will not always control the bleeding from the collaterals which often open into the aneurism or into the main trunks between the orifices in the sac and at the seat of ligature. This compels a more or less extensive dissection of the sac out of its bed as one of the necessary features of the procedure in order to secure all the collateral vessels that empty into the sac, unless the uncertain process of plugging the openings and packing the sac itself is resorted to. If the sac is dissected, as is usually done to secure the collaterals, the diffi-

culties of the operation are increased and the vitality of the limb is endangered by interfering with the collateral circulation which, in many types of aneurism, is most freely developed in the neighborhood of the sac. (*b*) Another serious objection to the old Antyllian operation as usually performed is that the sac is allowed to remain as an open cavity in the bottom of the wound, where it is packed or drained and allowed to heal by granulation. This invites infection, suppuration, and its attendant dangers of secondary hemorrhage; all that is obviated by the author's method of endo-aneurismorrhaphy, which does not disturb the sac from its vascular connections, and favors its prompt obliteration by insuring the infolded walls of the sac and keeping them in direct and close approximation. (7) The uncertainties and dangers of extirpation of the sac (Purmann's operation) are even more apparent than those of the Antyllus operation, because, in addition to the greater technical difficulties of extirpation, there is much greater risk of injury to the accompanying satellite veins and nerves which blend most intimately with the sac and often compel the operator to limit his intervention to a partial extirpation, leaving behind a considerable portion of the sac wall in order to avoid injury to important adherent structures. The greatest objection to extirpation, however, lies in the decided interference with the collateral circulation in the immediate vicinity of the aneurism, which entails a considerable risk of mortification in the distal parts. All these dangers are reduced to a safe minimum and are largely eliminated by simply obliterating the sac instead of extirpating it.

Remarks on a Second Series of Fifty Cases of Recurrent Appendicitis Treated by Operation.—SOUTHAM (*British Medical Journal*, January 10, 1903) states that this second series consists of 50 cases, of which 39 were males and 11 were females, the ages varying between ten and fifty-three years. In 5 cases there had been only one distinct attack, in 10 cases there had been two well-marked attacks, and in the remaining 35 cases three or more attacks. In almost every case the lumen of the appendix was either partially or completely occluded at some point in its course; sometimes close to its origin from the cæcum, sometimes at its middle or distal third. Though in most cases the walls were thickened, in a few, where the appendix was distended with fluid, they were extremely thinned. In one case, where the distention was extreme and the fluid contents were clear and watery, the appendix was quite translucent. It was frequently kinked or bent on itself at a right angle, and fixed in this position by adhesions which were present in the majority of cases, often firmer and more extensive after a few than after numerous attacks. In 3 of the cases collections of pus were found shut off in the distal portion of the appendix, which was dilated into a small cyst. In 6 cases there were fecal concretions, while in the remaining cases the contents consisted of a mucoid or mucopurulent fluid, which was sometimes mixed with fecal matter. In no case was any foreign body found. In 11 cases a localized suppuration had taken place outside the appendix, generally associated with a perforation of its wall. In 2 cases the patients had previously been operated on for appendicular abscess, and had had a recurrence of suppuration. These two cases illustrate the advisability of removing the appendix in all instances of suppuration—in recurrent as well as in first attacks—if this can

be effected without risk of breaking down the protective barrier of adhesions which shut off the collection of pus from the general peritoneal cavity. It is interesting to note that in many instances where marked lesions were found in the appendix there had been an absence of any local signs or symptoms during the quiescent periods between the attacks. Every case made a successful recovery from the operation.

Chloride of Ethyl in General Anæsthesia.—GIRARD (*Revue de Chir.*, November 10, 1902), after reviewing the subject in detail, states in conclusion: (1) General anæsthesia may be perfectly and completely obtained in man as well as in animals by chloride of ethyl. (2) Its action is rapid, it causes but slight excitement, and its application is made without resistance on the part of the patient, who awakes almost instantaneously after the withdrawal of the anæsthetic. (3) The rapidity of recovery demands that a close watch be kept by the anæsthetizer, and renders difficult a prolonged anæsthesia. (4) At the beginning of the anæsthesia it is important that the access of air to the respiratory tract be reduced to a minimum, and so a choice should be made of a good apparatus for inhalation. (5) The absence of nausea or vomiting after the cessation of anæsthesia makes this method the one to be preferred for all minor operations. (6) There is no need to fear any early accidents, for the absence of any irritant action upon the mucous membrane precludes any danger of reflex laryngitis. (7) However, it is necessary to watch for renal, hepatic, and cardiac lesions, as has been shown by pathological anatomy. This point should be cleared up before this method is generally used. (8) The mixed method seems to give the best results—shortening the pre-anæsthetic period, diminishing the amount of chloroform or ether required, suppressing of excitement at the beginning of anæsthesia and nausea or vomiting at the end; it possesses undeniable advantages and a certain superiority over simple anæsthesia. (9) The deaths which have been observed in animals after the anæsthesia has been established make it necessary to formulate certain reservations, for possible sudden depression of the respiratory centre may occur during the course of the anæsthesia (late syncope).

Surgical Intervention for Intestinal Perforation in the Course of a Case of Typhoid Fever; Recovery.—DEPAGE (*Jour. de Chir. et Annales de la Soc. Belge de Chir.*, November and December, 1902) states that this operation rests on a legitimate basis, as the statistics gathered by Boinet and Delenglade show that without operation 95 per cent. die, and that with operation the mortality varies between 79 and 88 per cent. Platt has collected from literature 103 cases of intervention, with 16 recoveries. The author's case was a woman of forty-two years of age, who presented the typical symptoms of perforation, and was operated upon three days after the perforation had occurred. A median incision under cocaine was made, and a collection of fetid pus was found on the side of the cæcum. Further exploration showed a small perforation in the small intestine about ten centimetres from the cæcum. A V-shaped resection of this portion of the intestine was then performed, the ends being joined in the usual manner. The intestines were then punctured with a small needle, so as to relieve them of a large accumulation

of gas, after which they were washed with hot sublimate solution, the focus of pus thoroughly washed out, and the abdominal wound closed, except at its inferior end, which was left open for drainage. The patient made an uninterrupted recovery. In conclusion the author states that an analysis of this case shows: (1) That perforation occurred at the twelfth or fifteenth day of the fever—that is to say, toward the end of the second week. (2) That the patient was not operated upon until three days after the perforation had occurred—that is to say, at the moment when the infection was general. The result in this case shows that even when the case seems perfectly hopeless it is, nevertheless, the duty of the surgeon to operate.

Note on the Value of Roux's Operation for the Radical Cure of Femoral Hernia.—RENTON (*British Medical Journal*, December 27, 1902) states that he has found this method satisfactory in the ten cases in which it was used. It consists in (1) making an incision over the crural canal; (2) isolation of the sac, putting a catgut ligature around its neck, and cutting it off; (3) a metal staple is passed obliquely through Poupart's ligament over the crural canal, taking care to avoid the femoral vein, and then it is gently hammered into the pubis; (4) stitching the skin incision. The author states that care must be taken not to put the staple in too tightly, which would injure Poupart's ligament; still, it must be sufficiently secured to prevent any recurrence of the hernia. The staple remains permanently in situ; it causes no irritation, and does not injure the bone. Roux has reported over sixty cases in which the retention of the staple has given rise to absolutely no trouble, and there has been no recurrence of the hernia.

THERAPEUTICS.

UNDER THE CHARGE OF

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Toxicology of Adrenalin.—DR. TARAMASIO reports on the toxic doses of adrenalin for frogs, guinea-pigs, and rabbits. Adrenalin was first prepared in 1901 by Takamine, following closely on Abel's work on epinephrin. It is a staple yellow powder, slightly soluble in water, and easily soluble in water of alcohol if acidulated with acetic or hydrochloric acid, and is considered to be by Takamine a basic salt with formula $C_{10}H_{15}NO_3$, but by Aldrich is thought to be $C_9H_{13}NO_3$. This drug gives a green color with ferric chloride, and a standard dilution of adrenalin has been fixed at that strength which

produces with a 15 per cent. solution of ferric chloride a green color only deep enough to last a few seconds, 1 c.c. of adrenalin solution so diluted, being called a ferric chloride unit. Thus one centigramme of the salt giving 700–750 ferric chloride units means that one centigramme dissolved in about 750 c.c. of water gives, with ferric chloride, a green tint which persists for ten seconds. Other preparations from suprarenal glands brought forward in previous years are: 1. Suprarenin, a red brown powder, which is a ferric compound introduced by Furth. 2. Epinephrin of Abel and Crawford, a benzol compound. 3. Sphygmogenine, a syrupy body, chemically indefinite, brought forward by Frankel. The second part of this report is taken up with the work of other men on the same subject. Many different animals have been used for experiment, but owing to different circumstances and the use of different preparations of the capsules it was impossible to gauge the dose of active substance which has toxic effects in each case. The author notes that Gourfein has said the toxic dose is very inconstant, but he finds but little variation in the fatal dose. In a general way, the results already arrived at are, that the blood pressure is greatly raised, the pulse is slowed, and respiration becomes more rapid and superficial. Pellicani is cited as the first to study the toxic action of suprarenal extract, thus finding that preparations from calves, oxen, and lambs are less toxic than those from carnivorous and smaller herbivorous animals; Oliver and Schäfer, as having rightly determined that vasoconstriction is due to a direct action on the smaller vessels, and is not of nervous origin, death being due, they considered, to bulbar paralysis, the respiratory centre being especially affected, and Cybulski (1896) as having brought forward pulmonary congestion as the direct cause of death. Finally, the work of Taramasio himself is given. He injected adrenalin dissolved in slightly acidulated water subcutaneously in the case of guinea-pigs and rabbits, and into the dorsal lymph sac in frogs. The following figures represent the dose of adrenalin injected per kilogramme of weight of the animal used for experiment:

	Dose never fatal.	Dose sometimes fatal.	Dose always fatal.
Frogs,	0.824 gram.	0.025 gram.	0.50 gram.
Guinea-pigs,	0.002 "	0.004 "	0.02 "
Rabbits,	0.002 "	0.004 "	0.01 "

Symptoms: dyspnœa, paresis with anæsthesia, and mydriasis in frogs appear a few minutes to an hour after injection, recovery, when it occurs, being complete within one, or at most, two days. Only six of the frogs treated with possible fatal doses died, though surroundings were unfavorable, the fact that pulmonary respiration is not necessary probably accounting for this slight toxicity, the skin taking on part of the functions of the lungs. Small doses cause slight increase of respiration in guinea-pigs, together with a slight fall of temperature, the prominence of the symptoms increasing in proportion to the dose. Sensation and motor power diminishing, death occurs generally within half an hour, and recovery, when occurring, being complete within a day. A blood-stained froth comes from the mouth and nose in the death agony, the heart continuing to beat after respiration has ceased. The lungs are found congested and covered with widespread ecchymoses, and acute œdema is the cause of death without doubt. The action of the drug

on rabbits, he states, closely resembles that on guinea-pigs; subcutaneous injection in both causing a slight slough, with a resulting scar, which is probably due to local anæmia, caused by contraction of the muscle walls of small arteries, for the anæmia itself prevents a rapid absorption from the point of injection. The author agrees with those who think pulmonary œdema causes death rather than with those who consider it a result of paralysis of the nervous system, though the latter action may be present to some degree in mammals, it plays a minor part. In frogs, on the other hand, the paralysis of the nervous system is thought to be the cause.—*Revue medicale de la Suisse Romande*, 1902, vol. xxii. p. 589.

Anæsthesin.—Dr. Chevalier reports on a new product, first discovered by Ritsert in 1890, but abandoned by him until recently, when Van Noorden, Dunbar, Lengemann and others have used it extensively, with excellent results. It is an ethylic ether of paramidobenzoic acid, and exists as a white powder without taste or odor; soluble with difficulty in 800 parts of water, but freely soluble in alcohol, ether, chloroform, acetone, fats, and oils. It is particularly adaptable in fatty combinations. Its dangers, if any, are due to its property of causing fixation of oxygen and the formation of methæmoglobinuria; but this takes place, according to Binz, in enormous doses only. Therapeutically it has been used with good results in ulcer of the stomach, gastric hyperæsthesia, in doses of thirty grains daily. In gastric irritability, doses of three to four grains prove efficient. In hyperæsthesia of the larynx it is used to advantage as a spray or as an inhalant, a 10 per cent. solution being used, oily or alcoholic. As a suppository in three to five-grain doses it is efficient in hemorrhoids. In a 10 per cent. lanoline ointment it has proven of inestimable service in a diabetic. Anæsthesin hydrochlorate may be employed hypodermically in 4 per cent. solution as an efficient local analgesic. Toxic or irritating effects have not been described.—*Revue de Therapeutique*, 1902, vol. lxix. p. 834.

The Active Principles of Rhubarb.—Drs. A. Tschirch and Henberger have restudied the question of the composition of rhubarb. Among the active principles they distinguish two groups of glycosides, tannoglycosides derived from rheotannic acid and anthraglycosides or anthracene glycosides. These pre-exist in the plant and are accompanied by a number of diverse products difficult to separate. The tannoglycosides are formed by the action of a left rotary sugar and of tannin (rhubarb red). The anthraglycosides are formed of the right rotary sugar and of different derivations of anthracene. Among these they mention chrysophanic acid, dioxymethylanthraquinone and trioxymethylanthraquinone, emodine, and rheine, which Tschirch thinks is a methyl ether of a tetramethylanthraquinone. All of these bodies are purgative.—*Pharmaceutische Zeitung*, 1902, vol. xviii. p. 547.

Treatment of Sydenham's Chorea by Arsenic.—Dr. P. Timacheff has made a careful analysis of arsenical therapy in twenty-six cases of chorea treated by arsenic in different combinations. In eight cases he used Fowler's solution, in six, Levico (an arsenical) water, in twelve he used an aqueous solution of arsenous acid after Comby's method. He preferred the last, both

from the standpoint of length of time of treatment and from the facility of administration. Among the many advantages of Comby's method of treatment there were also disadvantages. The most marked of these were the gastric and intestinal disturbances, nausea, and vomiting that were always present, and in rare instances diarrhœa follows. This nausea and vomiting was always the result of the ingestion of large doses of arsenic, and diminished on the withdrawal of the arsenic. The author's procedure was to give (1) as an initial dose one-half teaspoonful of the 10 per cent. solution, (2) increasing this half a teaspoonful a day (3) until a maximum dose of three to five teaspoonfuls a day was reached, (4) to continue this dosage for three to five days, according to the condition of the disease. Among the by-effects he noted herpes zoster in one, erythematous eruptions in two cases, and pruritus in one. Muscular soreness, paralysis, and paresis were not observed. As for recurrences, no arsenical therapy could prevent such.—*Medicinskore Obosrenie*, 1902, vol. xiv. p. 167 *et seq.*

Guaiacol Valerianate in Phthisis.—Dr. Kuhn administers this compound in doses of three to six grains in capsules or in drops with tincture of gentian. Stomachic disturbances may arise from the use of the gentian. In twenty instances ten showed marked improvement of appetite, in four there was a distinct lessening of the night sweats, in eight expectoration was diminished, twelve put on flesh. Tuberculous diarrhœa was not affected. The author concludes that combination possesses undeniable tonic properties, and is indicated in mild tuberculosis, in chronic bronchitis, and in bronchial dilatation.—*Therapeutische Monatshefte*, 1902, vol. xvi. p. 567.

PEDIATRICS.

UNDER THE CHARGE OF

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Tuberculous Meningitis, with Abnormal Onset.—E. Schlesinger (*Archiv f. Kinderheilkunde*, 1902, Bd. xxxiv., S. 355) reports a case under this title. The patient was a little girl, aged two and a-half years, whose brother had died a year before from tuberculous meningitis. The parents seemed to be in good health. The child, who had been in previous good health, suddenly became unconscious and developed violent convulsions, localized on the right side of the body, and affecting also the right side of the face. This condition, during which the temperature rose to $101\frac{3}{10}^{\circ}$, lasted for five hours. The convulsions then ceased, and were replaced by a hemiplegia of the right side, complicated by aphasia, and accompanied by dimi-

nution of cutaneous sensibility and exaggeration of the tendinous reflexes of the same side.

On the third day the palsy had completely disappeared, and, aside from anorexia, with slight elevation of temperature, the child seemed in her usual health. But some days later the temperature rose and remained between 100⅘° and 102°, while gradually the classic symptoms of tuberculous meningitis appeared (vomiting, convulsions, rigidity of the neck, stupor), and death occurred fifteen days after the onset of the first symptoms.

A Case of Cured Tuberculous Meningitis.—K. BARTH (*Münchener medicinische Wochenschrift*, 1902, No. 21, p. 877) adds another case to the few recorded instances of cure of proven tuberculous meningitis. The patient was a girl, aged thirty-two months, who, following an attack of measles, was seized with vomiting, accompanied by headache and high temperature. On the fourteenth day of illness the author observed dilatation of the pupils, which reacted sluggishly to light, slight stupor, pronounced rigidity of the neck, and the presence of Kernig's sign, but the scaphoid appearance of the abdomen was not present. The other organs were not affected, the urine contained neither sugar nor albumin.

With the diagnosis of meningitis, iodide of potassium was prescribed internally, with ice to the neck and head, and baths with cold affusions to the head. The fever was not characteristic. Headache became more and more intense, the pulse slow, and the respiration assumed a Cheyne-Stokes type. Later appeared tonic convulsions of the upper and lower extremities, with opisthotonos and incontinence of urine and feces. The cerebro-spinal fluid showed the presence of tubercle bacilli.

The author then decided to try bloodletting, and applied wet cups to the mastoid regions. Under the influence of this intervention the temperature fell and the headache ceased completely. Little by little the symptoms of meningitis disappeared; but for sometime deafness and psychic blindness remained, with extreme weakness of the lower extremities—symptoms which finally yielded to appropriate treatment. The duration of the illness was about six months.

[It is to be hoped that the further progress of this case will be reported after the lapse of a year or more.—ED.]

Rubella Scarlatinosa.—Under this caption FREDERICK C. CURTIS and HENRY L. K. SHAW (*The Medical News*, December 20, 1902) report an extensive outbreak of an eruptive disease in the village of Round Lake, Saratoga County, N. Y., beginning early in April, 1901, in the family of a farmer who supplied milk to the residents of the town. Three children were slightly ill, with a temperature of about 100° F., and with pulse from 80 to 90. The throats were congested in all three cases, and the glands of the neck were enlarged; there was an eruption extending uniformly over the chest, trunk, arms, and legs, bright red, and strikingly suggestive of scarlet fever. Two of the children had had undoubted scarlet fever a few years before. Nineteen days after his visit to these children a young man on a neighboring farm was taken ill with well-marked rubella, while his sister, twelve years old, exhibited a rash on the chest and back identical with that of the cases

in the first family. The face of the latter was clear, and while the throat was sore, the temperature was only 99⅘°, and the child did not feel ill. On the following day the first case appeared in the village, and next day six cases developed, and the disease spread with great rapidity. One hundred and forty-seven cases were seen, and others were known to exist.

When the disease appeared in the village the diagnosis of scarlet fever, which had been made in the first cases, was questioned, and Dr. Curtis, one of the authors, was called in consultation. The endemic character of the disease was very striking. No attempt was made to quarantine the individual patients or the town, yet only a few isolated cases developed in the nearby towns. In the opinion of the resident health officer there seems to be some ground for believing that the infection was carried in milk. The first cases appeared in the family of the man who supplied milk to the village, and all the cases, with a few exceptions, occurred in families thus supplied. No instance of a nursing baby having the disease was observed, and two or three infants fed on cow's milk from another farm were not infected. A majority of the patients were adults, fully 60 per cent.

The evidence presented in a study of this epidemic warrants the conclusion that it was rubella, largely of the scarlatinal form. The diagnosis from mild scarlet fever was quite sharply drawn. In conclusion, the authors deprecate the recognition of the "fourth disease" of Dukes, believing that everything that has been said by Dukes in describing the fourth disease can with equal truth be stated in regard to rubella.

The Bacteriology of Empyema in Children.—W. J. S. Bythell (*The Medical Chronicle*, Nov., 1902, p. 81) presents a study of forty consecutive cases of empyema, the object of which was to determine not only the species of bacteria present, together with their source and path of infection, but also the part played by the bacteriology in influencing the clinical course and termination of the disease.

While common in children of all ages (ten months to eleven years), fully twice as many boys as girls were affected. The pleura is infected in the great majority of cases by a process of direct invasion from a pulmonary lesion, which in children is usually a catarrhal pneumonia. In many cases which are apparently primary the source of infection is probably also an undiscovered patch of bronchopneumonia. The micro-organism by far most frequently present is the pneumococcus, which occurred in pure culture in 26 out of 40 cases. The streptococcus alone occurred in two cases, while one or other of these organisms was present in every case except one, in which was found Friedlander's bacillus and the staphylococcus albus.

The clinical results of empyema depend to some extent upon the species of bacteria found within the pleura, the pneumococcic cases being, on the whole, the mildest. This micro-organism may, however, give rise to very serious complications, either by direct invasion of surrounding viscera or by metastatic infection.

The bacteriological examination of the pus gives other indications as to the clinical prognosis which appear to be of considerable value: (*a*) A small number of poorly-stained micro-organisms which give feeble cultures usually denotes a good prognosis; (*b*) the reverse condition is not so frequently ac-

companied by severe clinical symptoms, especially when phagocytosis is well marked; (*c*) vigorous cultures are not in themselves a reliable sign of pathogenic activity.

The bronchial glands are probably invaded by micro-organisms from the pleural cavity in every case. The organisms are sometimes also found after death in the mesenteric glands.

With the exception of those cases in which there are tuberculous lesions of the pleura or lung, the best results may be expected from the resection of a rib with free drainage. In cases in which a tuberculous origin is suspected, removal of the fluid by paracentesis is to be preferred, and especially when the lungs are the seat of tuberculosis. Free drainage in these cases probably offers no better chance of cure than repeated aspiration, and the complete evacuation of the fluid by free drainage appears to accelerate the pulmonary lesion by removing the pressure upon the lung, while the prolonged use of a drainage greatly increases the danger of contamination from without.

Infantile Scorbutus and Sterilized Milk.—Recent communications to the Paris Société de Pédiatrie by MM. Thiercelin and Guinon, reporting cases of infantile scurvy in infants fed upon sterilized milk, have brought out a paper from NETTER (*Revue Mensuelle des Maladies de l'Enfance*, December, 1902, p. 543), who claims to have called attention to this point in etiology in November, 1898.

Since that time numerous observers have reported similar cases. In the collective investigation of the American Pediatric Society, published in 1898, in which 379 cases of scurvy were tabulated, 84 occurred in infants fed exclusively upon sterilized or pasteurized milk. In the same year von Starck published 67cases, collected in Schleswig-Holstein, of which 18 at least were due to sterilized milk. In the present paper the author tabulates 23 observations from French sources, of which nine followed the use of milk sterilized at home or at the dairy.

Admitting that fresh milk is possessed of antiscorbutic properties, and that under the influence of heat this quality is destroyed, the author reasons that, while we do not know all the elements to which fresh milk owes these properties, we do know at least one which is diminished in sterilized milk, and this is precisely the substance which is par excellence the preventive against scurvy—citric acid, the active principle of lemon juice. Various investigators have shown the presence in fresh milk of an important quantity of citric acid in the form of calcium citrate. Henkel states that cow's milk contains from 0.9 to 1.01 grammes of citric acid to the litre, and Göldner has shown that this acid is combined largely with calcium and, in very small proportions, with potassium and magnesium. Others have found this acid in the milk of other animals. Scheibe estimates the proportion per litre in human milk at 0.5 gramme, and in the milk of the goat at 1.5 grammes. According to Vaudin, this citric acid plays an important rôle in keeping the earthy phosphates in solution. In a word, as Corbette puts it, a litre of milk contains as much citric acid as an ordinary lemon. Corbette has also shown that the amorphous tribasic citrate of fresh milk is much more soluble when cold than when hot, and that under the influence of prolonged boiling it is transformed into the much less soluble crystalline citrate, which is precipi-

tated in large part and is only partially dissolved in cooling. The transformation and consequent loss of citric acid in solution will therefore be the more complete as sterilization is prolonged, as the cooling is less rapid, as the absence of subsequent agitation does not permit the redissolution of a part of the precipitated crystals. It seems certain that the milk of the cow normally holds a proportion of citric acid greater than the needs of the infant, since it is double that of human milk. It is therefore evident that even after sterilization cow's milk may preserve sufficient of its soluble citrates to prevent the development of scurvy, and that many infants may be fed upon sterilized milk, especially in the lesser dilutions, without developing scorbutic symptoms. But it is impossible to be assured that at any moment this balance may not be disturbed, owing to natural diminution in these antiscorbutics in the milk itself, or to greater prolongation of the sterilizing process. An observation of Medin's in 1898 at the children's hospital in Stockholm is very suggestive in this connection. Medin observed within a few months 15 cases of infantile scurvy in infants fed upon milk sterilized in the hospital by means of the Soxhlet apparatus, while in the preceding ten years not a case had been observed among the infants fed upon milk sterilized by the same method.

Attention is also called to the fact that milk is frequently subjected, not once but several times, to repeated cooking or sterilization. Neumann, in Berlin, in 1901 and 1902, collected a considerable number of cases of scurvy among families making use of a milk from an excellent dairy. It was found that, as a further precaution against contamination of the milk, the whole output of the dairy was regularly pasteurized before delivery to its consumers. As a result of Neumann's investigation, this dairy issued a circular to its patrons advising against further sterilization of the milk in the household, or that, at least, the time of ebullition in the sterilizer be reduced to one or two minutes at the most.

A later communication of von Starck (*Verhandlungen der Gesellschaft deutscher Naturforscher*, Hamburg, 1901) showed that infantile scurvy had become much rarer in Schleswig-Holstein since these facts had been recognized. Three years after his first investigation, in which 67 cases had been collected, a second inquiry among 300 physicians of the country obtained only 22 cases, 5 of which had been fed on maternized milk, 4 on sterilized milk (Soxhlet), 1 on sterilized milk, 2 on boiled milk, 2 on milk and barley soup, 4 on barley soup exclusively, and 2 on oatmeal soup.

While insisting upon the significance of citric acid contained normally in milk, and its diminution under the effect of heat, Netter is not convinced that the antiscorbutic properties of fresh milk are contained exclusively in its citrates. There are other antiscorbutic elements which are modified by heat or other agents, and it is extremely probable that they exist in milk.

In the infrequent cases of scurvy in infants nourished at the breast, the author believes that the mother's milk, under peculiar conditions, has lost to some considerable degree its antiscorbutic properties. Ill-health of the mother resulting from wasting disease, or other cause, such as prolonged mercurial treatment, may thus act in rendering her milk very poor in its antiscorbutic elements. In the case reported by Crandall in 1899 the mother had heart disease, with marked anæmia, and had been confined to bed since the baby's birth.

OBSTETRICS.

UNDER THE CHARGE OF

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The Efficiency of Disinfection of the Hands by Hot Water and Alcohol.—AHLFELD (*Monatsschrift für Geburtshülfe und Gynäkologie*, 1902, Band xvi. Heft 5) has long believed that the hands can be safely disinfected by the use of hot water and alcohol. He mentions a striking illustration, as follows:

He had occasion to induce labor in a patient with contracted pelvis, who had lost children by embryotomy. The case proved to be an obstinate one, and the child perished during the labor. The mother was taken with violent chills, followed by high temperature, and it was necessary to deliver the child by embryotomy. Although the head was opened the child failed to descend, and accordingly the abdomen was opened, the uterus incised, and the child delivered by Cæsarean section.

Great care was taken to disinfect the hands thoroughly with hot water and alcohol, and at the time when the uterus was opened basins containing hot water and alcohol were placed conveniently for the operator, and the hands were frequently rinsed in these fluids. Cultures from the body of the child revealed the presence of abundant staphylococci. The mother made an uninterrupted recovery, her temperature rapidly falling.

The alcohol employed was 96 per cent. in strength.

Two Cases of Pregnancy and Labor Complicated by Atresia and Stenosis of the Vagina.—KERMAUNER (*Monatsschrift für Geburtshülfe und Gynäkologie*, 1902, Band xvi., Heft 5) reports the case of a patient in her first labor, who had a protracted parturition, ending in the delivery of a dead child with forceps. A week after her confinement she had incontinence of urine, and examination showed a vesicovaginal fistula. The loss in substance was so great that extensive operation was necessary to restore the wall of the bladder. This reduced the size of the vagina very greatly. She came under observation when the second time pregnant.

On examination she was found to have a considerably contracted pelvis; the entrance to the vagina was much altered in size and shape, while the vulva had been practically closed by the preceding operation. When the patient came into labor she was delivered by Cæsarean section, with amputation of the uterus and extraperitoneal treatment of the stump. She made a good recovery, her child surviving.

The second case was that of a patient who, after her first confinement, lasting three days, recovered, with incontinence of urine and septic infection. A large vesicovaginal fistula had been repaired after her first labor.

She also had a considerably contracted pelvis, the external antero-posterior diameter being 17.5 centimetres.

On examination a double promontory was found with a true conjugate of 8.5 centimetres. The transverse diameters of the pelvis were normal. On examination the induction of labor was declined because it was thought that the head could pass through the pelvis, and it was believed that the scar tissue present would dilate at labor. It was thought best to allow the patient to come into labor spontaneously, and then, should the necessity arise, to perform Cæsarean section.

When labor occurred the head entered the pelvic brim transversely. An effort to dilate the scar tissue in the vagina by a Barnes bag failed, and Walcher's position was necessary to secure the insertion of the bag. Multiple incisions were made in the cervix to loosen the scar tissue, and a solution of cocaine was applied. Suppositories of opium were given, and the character of the pains became much better. The head gradually descended, the scar tissue was stretched, and under strong pressure upon the abdomen the head was born spontaneously. The child was slightly asphyxiated, but quickly revived and survived. There was no laceration found upon examination. The mother made an uninterrupted recovery.

The second case illustrates the extraordinary possibilities of spontaneous parturition. It must be observed, however, that this patient was in a hospital where interference could be undertaken at any time, and that every essential help was given to her labor by the use of drugs and by incisions in the cervix. It is evident that had the patient received no help her child must have perished, and quite possibly the mother also.

The Most Efficient Preparation of Ergot.—PALM (*Monatsschrift für Geburtshülfe und Gynäkologie*, 1902, Band xvi., Heft 5) analyzes the effect produced by different preparations of ergot, and has made personal observations and experiments to determine which of these is most advantageous. He believes that the efficient principle of ergot is largely chrysotoxin, and that sphacelotoxin is most advantageous of all these preparations. In subcutaneous administration the dose is from $\frac{1}{100}$ to $\frac{1}{10}$ of a drachm, which produces prompt uterine contractions. The remedy has little effect upon the general condition of the patient. Palm regards the hypodermic use of ergot as much superior to the administration of ordinary preparations by the mouth.

Cæsarean Section by Transverse Incision of the Fundus.—CURSCHMANN collected (*Monatsschrift für Geburtshülfe und Gynäkologie*, 1902, Band xvi., Heft 5) 119 cases of Cæsarean section by transverse incision of the fundus. He gives statistics to prove his belief that the transverse incision offers no essential advantage over the usual incision upon the anterior uterine wall. He supports his assertion by measurement of the uterine wall at the fundus, and, anteriorly, by a comparison of convalescence after the two methods and by minute study of the cases. The mortality was 12.1 per cent., or 13 cases, 11 of which were cases in which the uterus was retained, and 2 cases in which the uterus was removed. One patient was admitted to the hospital in a septic condition. The causes of death were as follows: Carcinoma of

the uterus, 1; purulent bronchitis, 1; embolism of the lung, 1; death from shock immediately after the operation, 1; peritonitis, 8. In 3 cases autopsy showed adhesions of coils of intestine with the uterine wound. This was also seen in several cases which recovered in which it was necessary to do abdominal section for the relief of obstruction of the intestine.

Repeated Cæsarean section was done in 10 cases, in 8 of which the first operation was made by longitudinal incision in the anterior uterine wall, while in two transverse incisions of the fundus had been practised. In all of these cases there was adhesion between the uterus and the abdominal wall and omentum. No scar in the uterus could be discovered in these cases. Of these 10 repeated sections, 7 recovered without fever, 1 had fever and recovered, and 1 died.

Hydatiform Mole, with the Report of 2 Cases and Collection of 210 Cases.—FINDLEY (*Medical News*, December 6, 1902) reports 2 cases of this condition and summarizes his study of the subject as follows:

The causation of hydatiform mole is unknown. It is most frequently found between the ages of twenty and thirty years, more often in multiparæ. It probably results from degeneration of the villi of the chorion through some disturbance of maternal circulation. The connective tissue stroma of the villi degenerates, with serous infiltration or œdema. The syncytium and Langhan's cells penetrate more deeply when maternal nutrition is defective. In 16 per cent. of cases malignant degeneration occurs. It is very difficult to draw the line between benign and malignant cases. The examination of a specimen gives but little information regarding it. Retention of a mole within the uterus does not influence its disposition to become malignant.

Diagnosis can only be positively made from seeing the vesicles. The most constant clinical point lies in the rapid development of the uterus, with irregular shape and consistency and hemorrhage.

The treatment of the condition consists in emptying the uterus at once. Because the womb is thin and weak it is best to avoid the use of the curette and to employ ergot and vaginal packs to control the hemorrhage and stimulate expulsion. After the mole is expelled, the uterus should be explored with the finger, irrigated and packed with iodoform gauze. Two weeks after the birth of the mole the uterus should be curetted, the scrapings examined, and if malignant disease is beginning, hysterectomy should be performed. The patient should be kept under observation for three years afterward, and should hemorrhage occur the uterus should be again curetted and the scrapings examined microscopically.

Statistics show the average age of these patients to be twenty-seven years, the extremes being thirteen and fifty-eight years. In one patient eleven moles developed. In 8 cases there was cystic degeneration of the ovaries. In 1 case the mole developed in the Fallopian tube. The longest period at which malignant disease occurred after the development of the mole was four and one-half years. The mortality of this condition is 25 per cent. The causes of death are: syncytioma malignum, 16 per cent.; hemorrhage, 4 per cent.; septic peritonitis, 2 per cent.; other causes making up the remainder.

GYNECOLOGY.

UNDER THE CHARGE OF

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Adenoma Malignum.—HERMANN (*Centralblatt für Gynäkologie*, 1903, No. 44) describes a case of cancer of the portio, which was admitted to Saenger's clinic as inoperable, the broad ligaments being involved. The treatment consisted in curettement and cauterization with chloride of zinc, which relieved the patient for six months, when it was necessary to repeat the operation on account of recurrence. She was relieved for another period of six months, when the same treatment was adopted. A profuse serous discharge persisted, but there was no return of the hemorrhages, which were profuse before the first curettement. Microscopic examination of the growth last removed showed an ordinary glandular formation of a benign type, offering a marked contrast to the malignant course of the disease.

The writer infers that the growth was a true malignant adenoma. Of the nineteen cases of malignant adenoma reported in the literature, seven were really adenocarcinoma. In the case reported the relatively benign character of the growth was shown by the fact that it had existed for seven years, yet the patient remained in good health. He suggests that the profuse mucous discharge, which never became purulent, may be regarded as an important point in the differential diagnosis between malignant adenoma and adenocarcinoma.

Vaginofixation and Ventrofixation.—DIRMOSER (*Centralblatt für Gynäkologie*, 1903, No. 44) reports sixty-nine cases of vaginofixation from Erlach's clinic in Vienna, in the majority of which Dührssen's method was adopted. Forty-one patients who were kept under observation were cured. Of the forty-nine cases of Dührssen's operation, one patient became pregnant and had a normal delivery. Of the seventeen in whom the round ligaments were shortened per vaginam, seven were subsequently delivered one or more times, and one aborted.

Ventrofixation was performed seventy-six times, fifty-eight patients being kept under observation. Four patients were delivered at term and two aborted.

Benign Epithelial Proliferation in the Corpus Uteri.—HENGGE (*Centralblatt für Gynäkologie*, 1903, No. 44) reports two cases of uterine hemorrhage in patients, aged forty-four and forty-nine years, in which tissue removed with the curette showed under the microscope circumscribed and diffuse epithelial growths, without loss of substance. In one case there was accom-

panying glandular hyperplasia. Pregnancy, cancer, and tuberculosis were positively excluded. There was also no evidence of an inflammatory process. No cause for the peculiar epithelial proliferation could be discovered; in fact, the writer regards these cases as unique.

Leucocytosis in Pelvic Suppuration.—DÜTZMANN (*Centralblatt für Gynäkologie*, 1903, No. 47) reports 165 cases in which he was enabled to establish the presence of pus in the pelvis before operation. Pus was never found when the blood count was normal. The writer was even able to infer the cause of the suppuration from the number of leucocytes, a count of 20,000 to 30,000 pointing to streptococcus infection, while one of from 11,000 to 13,000 was commonly associated with the presence of gonococci or colon bacilli. In peritonitis and septic infection an increase in the leucocytes is a favorable sign, even in the presence of persistent elevation of temperature. If, on the contrary, there is no increase while the temperature is high, a fatal termination may be expected; this is probably due to deficient phagocytosis.

Alcohol as a Disinfectant.—SCHAEFFER (*Centralblatt für Gynäkologie*, 1903, No. 47) believes that it is impossible to render the hands sterile by any method of disinfection. After repeated experiments, he finds that by scrubbing for five or ten minutes with green soap and for five minutes with absolute alcohol the best results are obtained. It is, however, necessary to change the alcohol after each washing. Moreover, the germ-destroying action of the alcohol is lost in a few minutes if the hands are immersed in watery fluids, blood, or serum.

The principal value of alcohol, in the writer's opinion, is its power of removing fat and epithelium—that is, its mechanical purifying action.

Vaginal Hysterectomy.—NIGRISOLI (*Centralblatt für Gynäkologie*, 1903, No. 46) reports 462 vaginal hysterectomies with 11 deaths (2.38 per cent.). Of these, 55 operations were performed for cancer, with 4 deaths; 14 abdominal hysterectomies were done for cancer with 2 deaths. The writer now prefers the abdominal route in all cases, except when the uterus is prolapsed and the disease is absolutely limited to the organ. Seven patients, operated upon before 1898 and 5 since then, were still without recurrence.

There were 56 vaginal hysterectomies for fibromyoma, with 1 death, and 98 abdominal, with 8 deaths; 41 cases of ectopic gestation (25 operated upon per vaginam) were all successful; 274 radical vaginal operations for diseased adnexa were followed by a mortality of 5, and 300 abdominal resulted in 18 deaths. Only 1 fatal case is noted in 168 vaginal sections for the evacuation of pus; in 75 abdominal sections for the same condition there were 10 deaths. In 34 conservative vaginal sections there was no mortality.

The writer used the angiotribe in 50 cases, but always employed ligatures in addition.

Vaginal Ovariotomy.—HEINSIUS (*Centralblatt für Gynäkologie*, 1903, No. 46) reports 700 cases of colpotomy in the Greifswald clinic during the last three and one-half years. Of these, in 110 oöphorectomy was performed,

the anterior incision being preferred, as it is believed that the parts are rendered more accessible. Five deaths resulted, 3 due to the escape of pus, and 2 to improper catgut. Martin's mortality in 262 vaginal cœliotomies was only 3 per cent.

The writer believes that this is the ideal method of removing small tumors which are not adherent above the true pelvis. Cystic tumors as large as a man's head can be removed in this way, but it is not advisable to attempt the removal of solid growths larger than the fist.

Ovarian Parotitis.—TROITZKY (*Ronsk. Wratch; La Gynécologie*, 1902, No. 5) reports a peculiar epidemic of mumps in a boarding-school, in which one-third of the patients complained of pain in the ovaries as well as in the parotids. When only one parotid was affected the ovary in the corresponding side was tender; both ovaries were attacked simultaneously with both parotids. The ovarian pain and tenderness developed after the parotid swelling and diminished progressively with the latter. In girls who menstruated no menstrual or mammary disturbance was noted. The writer infers that although oöphoritis is a rare complication of mumps as compared with orchitis, it is doubtless more common than is usually supposed, being overlooked on account of the situation of the ovary and the difficulty of examining it.

The exact nature of the anatomical changes is not positively known, but it may be inferred that there is either a perioöphoritis or a parenchymatous inflammation analogous to that observed in other infectious febrile diseases. It usually occurs in girls above ten years of age. The possibility of this complication of mumps should always be borne in mind, and if ovarian symptoms appear suitable treatment should be instituted.

Radical Operation for Cancer of the Uterus.—KLEINHANS (*Centralblatt für Gynäkologie*, 1903, No. 43) reports thirty-two cases of radical abdominal hysterectomy, with three deaths. He curettes and cauterizes freely and clamps off the vagina before opening the abdomen. In cases of cancer of the cervical canal he prefers amputation. All glands which can be felt are removed, since, according to different observers, from 27 to 57 per cent. are cancerous. The writer believes, with Rosthow, that the glands are early involved. It is often very difficult to determine before operation whether indurations of the broad ligaments are inflammatory or malignant. Sometimes an exploratory laparotomy is necessary in order to determine this point.

Cancer of the Uterus.—POZZI (*La Gynécologie*, 1902, No. 5) concludes his paper read before the International Medical Congress with the following deductions: 1. The surgical treatment of uterine cancer rarely insures relief extending beyond two years. 2. Hysterectomy is not justifiable if the uterus is fixed by indurations in the surrounding tissues. 3. The importance of infection of the lymph nodes has been exaggerated, since recurrence usually takes place in the cicatrix; hence extirpation of the glands, even when it is supposed to be complete, seems to have little influence on the return of the disease. 4. Abdominal hysterectomy is a more

serious operation than vaginal, on account of the greater risks of infection, and should be reserved for special cases in which the vagina is narrow, the uterine wall softened, or the cul-de-sac extensively involved; also, when the uterus is unusually large or complications are present—fibroids, pregnancy, pyometra, or pyosalpinx. In a few instances the abdominal route may be preferable, in order to dissect out the uterus from the diseased tissues. 5. Vaginal hysterectomy is accordingly preferable on account of the smaller risk, the ease with which it may be performed in the early stage of the disease, and the fact that even a palliative operation is preferable to a "pseudocurative" one in which the chances of an immediately fatal result are so great.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

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Sarcoma of Branchial Cleft.—Dr. James E. Newcomb, of New York, reports this case (*Medical News*, October 26, 1901), which occurred in a man, aged sixty-five years. Two years previously he noticed a swelling on the right side of the palate, with a soreness in the gums adjacent. The swelling gradually increased for a year when it was lanced, giving escape to thin, clear fluid, with permanent subsidence of the pain. Lancing had to be repeated several times on account of recurrent swelling. The growth was removed by Dr. Weir through an external incision. A bluish, cystic tumor, reaching upward almost to the base of the skull, was carefully shelled out. It was about the size of a mandarin orange, on one side of which was a solid mass, in size and shape resembling a tonsil. The report of the examination at the laboratory of the Columbia University Medical School read: "Telangiectatic sarcoma of the branchial cleft, with hyaline degeneration; lymph nodes hyperplastic; no tonsillar tissue."

True Papilloma of the Nasal Septum.—Dr. James E. Newcomb, of New York, reports (*Ibid.*) a case of true papilloma of the left side of the septum in a man, aged fifty-five years. The case had been sent to him on account of severe epistaxis, which was found to be due to a large erosion on the convex of the septum, which was strongly bulged to the right. Some bibliographic references accompany the report.

Morbid Growths of the Nose: Osteosarcoma of the Inferior Turbinate.—Dr. James E. Newcomb, of New York, reports (*Medical News*, October 26, 1901) a case in a colored male subject, aged forty-one years, who had had an increasing obstruction in the right nasal passage for some four

months, but without pain or hemorrhage. A bony adhesion was found between the inferior turbinate and the septum, which was removed with the trephine. Recurrence ensuing a few weeks later, the core of tissue was removed with the trephine and found by Dr. Jonathan Wright to be an osteosarcoma. Further treatment was not allowed.

Angiofibroma of the Nose.—This case was reported by DR. NEWCOMB (*Ibid.*), which occurred in an Irish-American, aged twenty years, who for seven months had complained of alternating nasal obstruction, finally becoming permanent, on the left side. Inspection revealed an apparent polyp hanging from the middle turbinate, but posterior rhinoscopy disclosed a mass in the rhinopharynx, apparently blocking the left side only. The anterior growth was so hard that it resisted the cold wire snare, bleeding freely. A small portion removed with considerable hemorrhage, which was checked with difficulty, was found microscopically to be an angiomatous fibroma. Its point of origin could not be determined, and the patient refused further surgical interference.

Nasal Polypi the Cause of Atrophy of the Optic Nerves.—At a recent meeting of the French Society of Ophthalmology (*Archives de Médécine et de Chirurgie Speciales*, May, 1902), DR. PARISOTTI reported a case of a young man, aged twenty-five years, whose vision rapidly diminished to 1/50 on the right and 1/10 on the left, the papillæ becoming pale and almost on the point of being completely blanched. Rhinoscopic examination was at first negative, but subsequently revealed hypertrophy of the turbinates, and polypoid vegetations of the middle meatus. After the ablation of these growths vision increased progressively, so that five months later it equalled I in both eyes, the papillæ remaining very white. Six months later, however, vision had receded to 4/10. The author attributes these optic troubles to a spasmodic ischæmia produced by the nasal vegetations.

Foreign Body in the Larynx.—DR. OLIVER A. BLUMENTHAL, of Syracuse, N. Y., reports (*American Medicine*, August 30, 1902) a case of a triangular fragment of bone one and one-half inches long impacted in the larynx; the sharp-pointed end was in the left arytenoepiglottic fold and the broad end in the right fold. The bone was released and extracted with laryngeal forceps under guidance by the laryngoscopic mirror.

Morbid Growths of the Larynx.—DR. JOSEPH D. BRYANT, of New York, reports (*Journal of the American Medical Association*, October 18, 1902) an interesting case in a patient, aged forty-five years, of a large tumor of the posterior wall of the larynx low down, removed by enucleation after external access by low lateral pharyngotomy. It weighed 425 grains, and was $1\frac{1}{2} \times 1\frac{3}{4} \times 1\frac{1}{2}$ inches in its antero-posterior, vertical, and transverse diameters, respectively. Muscular fibres were found in the structure, leading to the surmise that it must have originated in muscular tissue. The lateral pharyngotomy was selected because digital exploration had revealed an apparent attachment of the tumor to the right portion of the pharyngeal wall. When exposed to digital exploration through the external wound,

the growth was found quite immovable and apparently firmly attached to the posterior wall of the pharynx. The finger, introduced through an incision between the tumor and the mucous membrane covering it, completely enucleated the growth, leaving its entire membranous envelope intact. The patient made a good recovery. A number of somewhat similar instances were reported by gentlemen who took part in the discussion of this paper before the Section on Surgery and Anatomy of the American Medical Association at its fifty-third annual meeting.

Foreign Bodies in the Air Passages: Escape of the Outer Tube of a Durham Tracheal Canula.—Dr. E. D. Ferguson, of Troy, N. Y., reports (*New York State Journal of Medicine*, October, 1902) the escape into the right bronchus of the outer tube of a Durham double canula in consequence of the neglect of the manufacturer to provide it with the necessary protective flange at its outer extremity. Its removal was effected by incising the tracheal wall down toward the bifurcation, when, with the finger, the missing tube was felt in the right bronchus, the upper extremity being well within the bronchus. With the aid of illumination from a head mirror the upper edge of the tube was seen, and it was removed with forceps.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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Multiple Progressive Hyaloserositis (*Studies from the Royal Victoria Hospital*, Montreal, vol. i., No. 3).—Under the foregoing title Nichols discusses the etiology, morbid anatomy, and clinical aspects of that form of a chronic proliferative process affecting serous surfaces "characterized by the formation of a membrane composed of dense layers of connective tissue of a peculiar cartilaginous appearance." This membrane, which may be several centimetres in thickness, is a continuous stratified layer, and can be peeled off from the subjacent affected organs. The upper part of the peritoneum, particularly the liver and spleen capsules, the bases of the pleural cavities, and the pericardium are the parts oftenest involved. As a result, the structures attacked may show atrophic, degenerative, or even fibroid changes.

As a localized liver lesion the process has been described as chronic hyperplastic perihepatitis, chronic deforming perihepatitis, and by Curschmann as

the "zuckerguss" or iced liver, from the porcelain-like or "frosted" appearance. Though the liver may be primarily and solely involved, the process is usually progressive, affecting the serous surfaces consecutively, but all may not show the peculiar "icing" appearance. The main theories as to the causation of the process are pericarditic pseudocirrhosis (Pick), chronic nephritis (Hale White), and inflammation (Curschmann).

From a careful study of his own and thirteen reported cases of "zuckerguss" liver, Nichols would prove that the first two hypotheses are incorrect. Reasoning from the clinical and pathological evidences at hand, he concludes that the etiological factor is a chronic inflammatory process caused by some micro-organism of slight virulence. The tubercle bacillus is capable of producing quite similar but still distinct lesions.

The pathological findings make clear many of the clinical manifestations. Ascites is constant; anasarca and emaciation are common. The great omentum is often contracted and indurated. The liver, which is usually almost completely invested by the frosted membrane, is generally small and deformed, with round edges and a smooth surface. In the great majority of cases there is no cirrhosis; there are, however, fatty and parenchymatous changes and passive congestion. The gall-bladder is frequently involved in the perihepatitis. The right pleural cavity is more frequently seriously involved than the left. This is strikingly more common at the base of the right lung, the central tendon of the diaphragm, and the right side of the pericardium. Chronic adhesive pericarditis is usually present; the pulmonary and cardiac changes are what would be expected under the conditions. The spleen, which is commonly enlarged, is often frosted, particularly when there is left-sided pleural involvement. It may be atrophic in advanced cases. No special abnormality appears in the kidneys. An acute terminal infection of many of the serous sacs or of the lungs is frequent.

Histologically, this "icing" is found to be a laminated fibrous tissue, with more or less hyaline transformation and giving evidence of being an organized inflammatory exudate.

Clinically, only the cases with the frosted liver are found to admit of diagnosis, and the symptoms vary considerably according as the liver is primarily or secondarily affected.

The average age of onset is about thirty years; the duration varies from two to sixteen years, averaging six years. The sexes appear to be about equally affected. The onset may be either acute or very insidious. The primary infection is most frequently in the pericardium, next in or about the liver, and less often some other peritoneal inflammation. Alcohol, gout, and syphilis appear to have little and heredity absolutely no etiological significance. The constant and striking physical sign is the extreme ascites requiring repeated paracentesis. The ascitic fluid is straw-colored, of a specific gravity of less than 1010, but twice as rich in albumin as a transudate, which is cited as evidence of its inflammatory causation.

If the process is primarily pericarditic anasarca appears first, then a train of symptoms following the extension of the inflammatory process to the liver *via* the right pleural cavity, and finally the ascites. If the liver is primarily involved there is epigastric pain, sense of fulness in the abdomen, and dyspnœa, followed by a slowly developing ascites, and then perhaps an ex-

tension to the right pleura and pericardium, with consequent clinical signs and symptoms. Icterus is not present in uncomplicated cases. The urine is decreased in amount, and albumin is commonly absent. The prognosis is eventually hopeless. The treatment is purely symptomatic. Unusual precaution should be taken against exposure to acute infections.—J. L. Y.

The Intestinal Origin of the So-called "Fever of Infancy" (Fiebre de Borras).—DUENAS (*Revista medica Cubana*, January, 1903, No. 1) suggests the possible relation of this Cuban infantile fever with the summer diarrhœa of infants of the United States. The recent work of Duval and Bassett has shown that at least certain forms of summer diarrhœa of children are due to the bacillus dysenteriæ of Shiga, as shown by the presence of this organism in the stools of such cases and the agglutination reactions on the organism with the blood of those ill of or convalescent from the disease.

In a case of the author's, a girl of twenty months, who had been suffering for several days with persistent bloody vomiting, pain in the epigastrium, and mucus and ill-smelling stools, a distinct fever and rapid pulse, the patient's blood twenty days after the beginning of the disease gave a positive reaction with the bacillus dysenteriæ in dilutions of 1:60. This case the author further regards as significant of the possible relation of this bacillus with certain of the "black vomits" attended with fever and of unknown etiology.—F. P. G.

The Inheritance and Intra-uterine Transmission of the Agglutinating Properties of the Blood and the Formation of Agglutinins in the Bodies of Embryos.—JUREWITSCH (*Cent. f. Bac. u. Para.*, 1902, Bd. xxxiii. p. 76) states that the agglutinating properties of the blood of normal pregnant rabbits and guinea-pigs for typhoid bacilli was first determined. The blood of some normal rabbits possessed this power in 1:80 dilutions. The blood of the young from such mothers also had the power to agglutinate typhoid bacilli, but in less degree than the mothers. Occasionally in a litter from a single mother certain animals showed agglutinins in their blood, while others did not. With normal guinea-pigs neither the blood of mothers nor young showed any tendency to agglutinate typhoid bacilli. Normal pregnant guinea-pigs were now immunized against typhoid bacilli during the time of pregnancy, so that at the birth of the young agglutination took place with the mother's blood in 1:4000 or 1:5000 dilutions. In three out of thirty-one cases no agglutination could be demonstrated in the young. In all the other cases agglutination was obtained with the blood of the young, but was three to thirty times weaker than with the blood of the mothers, and after a short period the blood of the young lost this property entirely. In order to determine whether the agglutinins were simply transmitted through the placenta to the blood of the young, or whether the fœtus was actually endowed with the power of producing agglutinins, the mothers were subjected to a passive immunity, and agglutinating sera from previously immunized guinea-pigs, rabbits, and horses were injected into the pregnant mothers. After a few hours Cæsarean section was performed and the blood of the young tested. The result was the same as when the mothers were immunized during pregnancy. It was further found that the blood of young normal rabbits coming from a

normal mother whose blood agglutinated typhoid bacilli did not lose their agglutinating properties as they grew older, but, on the other hand, showed in some instances agglutination in higher dilutions than the mother's blood. The author believes these animals inherit the power of producing agglutinins. Guinea-pigs which had previously been immunized were allowed to become pregnant. The young of these animals showed the power of agglutinating typhoid bacilli often in much higher dilutions than the mothers.—W. T. L.

A Contribution to the Knowledge of the Pathological Changes Following Thyroid Extirpation in Rabbits.—BENSEN (*Virch. Arch.*, 1902, Bd. clxx. p. 229) states that the experiments may be divided into three groups: First, rabbits from which the thyroids had not been removed were fed upon thyroid extract; second, the thyroid gland was removed and no thyroid extract given; and, third, the thyroid gland was removed and animals then fed upon thyroid extract. In each series of experiments the animals were killed after a certain number of days and the thoracic and abdominal organs examined. In the first group the animals were killed after receiving 0.3 grain of thyroid extract twice daily for twenty-four days. Sections of the liver showed fatty infiltration and hyperæmia. Colloid droplets were found in the convoluted tubules of the kidney. The pathological changes were, however, not very marked in any organ. In the second group of experiments extensive degenerative changes were found in the kidneys, liver, and heart muscle. In animals that lived thirty to forty days after the operation the kidney tubules were filled with enormous amounts of colloid, sometimes appearing in long cylinders, and if life was prolonged from 100 to 150 days there was, besides the presence of colloid, such an extreme grade of degeneration of the kidney epithelium that even the nuclei were much affected. The liver and heart muscle showed the same general type of extreme cellular degeneration. In those animals living longest proliferative changes were noted in the kidney and liver. Infiltration of leucocytes sometimes occurred in the liver. The splenic changes consisted principally in hyperæmia and pigmentation. No alterations were observed in the stomach, pancreas, parotid gland, tongue, adrenal, and generative organs. In the third group of experiments changes similar to those first described were found, but in much less degree. The author concludes that when the thyroid glands of rabbits are extirpated a poison is either produced or withheld in the body which gives rise to a peculiar degeneration of the cells of the kidney, liver, and heart muscle. The product of this cell degeneration appears as colloid droplets or in the kidney tubules even as long colloid cylinders.—W. T. L.

The Relations Between the Lymphatics and the Connective Tissue.—W. G. MACCALLUM (*Johns Hopkins Hospital Bulletin*, 1903, vol. xiv. p. 1) says: By means of silver staining, v. Recklinghausen, in 1862, showed that the walls of the lymphatic capillaries are composed of a single definite layer of flat polygonal endothelial cells. He supposed, however, that the walls were incomplete and that the lymphatics were in direct communication with the intercellular spaces of the surrounding tissues. Hiss, Teichmann and others opposed the idea of the lymph canaliculi, and believed in the integrity of the lymph vessels. MacCallum has studied by means of injections, and silver stains the lymphatics of the skin of embryo pigs. In sections

stained with hæmatoxylin and eosin the lymphatics could be readily made out as vessels wide in comparison to the capillaries, and lined by a single layer of cells with clear protoplasm and flattened-out nuclei. A fine black line surrounded each of these cells in silver stains. Clear spaces were seen in the surrounding tissue, and often lay next to the clear endothelial cells of the lymph capillaries. The resulting appearance was that of an apparent opening in the wall of the lymphatics. That this was not actually the case could be shown in silver stains, followed by a nuclear stain where the intercellular spaces stained black and surrounded the clear spaces, each one of which proved to be a clear cell with central nucleus. These cells were branching, and without the nuclear stain suggested anastomosing channels. When the lymphatics were injected with silver solution the lymphatic vessels stood out in sections as a network of smooth-walled vessels, with a quite perfect lining of tessellated endothelial cells, and the intervening and surrounding tissue was not stained. From these observations the author concludes that the lymph canaliculi or "saft kanälchen" of Recklinghausen cannot be injected or in any other way demonstrated to be in connection with the lymphatics, but are cells whose outlines are stained with silver nitrate. When the lymphatics were injected with methylene blue, small extravasations of the blue fluid occurred along the course of the vessel if much force was used. Under the microscope these extravasations took place in a sudden explosive manner, and when pressure was made upon the specimen the lymphatics were emptied, but the extravasations were left unchanged. The process of development of the lymphatics appeared analogous to that of the bloodvessels. Sprouts of single cells or of several cells projected from the lymph vessels, and sometimes bridges of cells connected two vessels. The lumen was apparently formed by separation of parallel cells or from the hollowing out of a single cell. Experiments to determine the manner of transporting foreign granules showed that the process was carried on, as far as could be determined, entirely by phagocytic cells. Injections of granular material were made into the subcutaneous tissues of rabbits, and in sections made several days later through the lymphatic trunks relatively little free pigment was found. Almost all the granules were inclosed in cells.—W. T. L.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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Ptomaine Poisoning.—From time to time cases of several members of a family, or a number of families suffering from acute poisoning after eating tinned meats, frozen rabbits, etc., are reported in the public press, and

within the last few months they have been of rather frequent occurrence; but none has surpassed in severity and extent one in which nearly two hundred persons in widely distant parts of the country were attacked with pains, purging, and vomiting, with alarming prostration, and in several cases a fatal termination, after partaking of pork pies bought at or about the same time from one of the best shops in Derby. The manufacture of pork pies is the staple industry of Melton Mowbray, in Leicestershire, and these enjoy a European reputation; but those of many other makers in the north midlands are in no way inferior, and among them those of the firm in question stand deservedly high. There was nothing in the taste or appearance of the pies to arouse suspicion, but Professor Délépine found a bacillus resembling the B. enteritidis of Gaertner—in fact, that known as the B. Friedebergensis of Gaffky—and succeeded in extracting from the jelly a toxin fatal to guinea-pigs and rabbits. In this instance the poisonous character was common to the whole of the pies or to a large number of them, made at the same time, and must therefore be ascribed to the condition of the carcasses or to some unknown accident incident to the preparation of the pies in general, whereas it is more often peculiar to one among many.

Probably the most remarkable example of ptomaine poisoning was one reported in 1892 by the late Dr. E. Gwynn, Medical Officer of Health of Hampstead, and absolutely unique in its virulence. The food in this instance was one of the well-known Paysandu tongues, which a gentleman, his wife, and two children were about to partake of for breakfast. On opening the tin they remarked its somewhat dry appearance and the absence of jelly. He, noticing something unpleasant in the smell, forbade them to eat it, and proceeded to divide an omelette among them, using for this purpose the same fork. The wife and elder child, who had just tasted but had not swallowed the tongue, were seized about noon with symptoms closely simulating those of Asiatic cholera—pain, vomiting, involuntary watery evacuations, and collapse—the mother being for some hours cold, pulseless, and unconscious. The father and the other child, who had not tasted the tongue, and had merely eaten the omelette touched with the infected fork, were attacked in the afternoon with vomiting and faintness, and the child sank into a profound stupor, from which she could not be aroused for some hours. They all ultimately recovered, but for some time the life of the lady had been almost despaired of. Mr. Stokes, the analyst, found parts of the tongue softened, acid, and charged with tin and iron dissolved by the acid. Professor Macfadyen obtained therefrom cultures of the usual bacteria of putrefaction. Mr. Stokes' assistant, who put into his mouth a piece the size of a shilling, "to see how it tasted," suffered from vomiting and giddiness for thirty hours. Mr. Wynter Blyth endeavored by Brieger's method to extract some alkaloids, but without success, and the results of injections of solutions of the extract on guinea-pigs were negative, from which he concluded that the poison was a toxalbumin or enzyme—bodies at once the most virulent and the most unstable, and which had disappeared in the interval of five days that had elapsed between the opening of the tin and his experiments. He expressed the opinion that the failure of the most careful investigations after inquests on undoubted cases of meat poisoning may be thus explained.

Scurvy: A Chronic Ptomaine Poisoning.—The etiology of scurvy had long been one of the most obscure and vexing problems in pathology; but the hypothesis put forward a few years ago by Professor Tomp, of the University of Christiana, and advocated by MR. KOETTLITZ, Medical Officer to the Jackson Harmsworth Arctic Expedition, in the *British Medical Journal*, February 8, 1902, offers the only rational explanation, reconciling and rendering intelligible many apparently conflicting facts and experiences. Tomp and Koettlitz maintain that scurvy is nothing more or less than a chronic poisoning by ptomaines formed by certain bacteria in imperfectly preserved foods. Other factors may conduce to the production of the disease, not, indeed, as efficient causes, but as predisposing conditions, especially by diminishing the power of resisting or of destroying the poisons; and the well-known, though not infallible, prophylactic action of lime juice may be due to its in some way neutralizing or antagonizing the toxins.

It is a fact that a continuous diet of salt beef or pickled pork, especially when these preserved meats have been kept for many months, is almost inevitably followed by the appearance of scurvy in a ship's crew, and that it never arises among those who enjoy a diet of fresh meat, vegetables, and fruit, and rarely when, in default of these, or when they can be supplied at intervals only, the diet consists of good tinned meats and vegetables, with the addition of sound dried fruits, vegetables, with potatoes and lime juice.

Other organic acids, even vinegar, are reputed to possess some antiscorbutic properties, and Dr. Neale, of the steamship Eira, claimed for draughts of fresh blood the exemption of the crew.

But in some Arctic expeditions in which the food was entirely or almost entirely preserved, but by the absolute exclusion of the air after complete sterilization, as those of Professor Nordenskjold and Dr. Nansen, not a trace of scurvy appeared in the course of three or four years. More striking still was the experience of the Jackson Harmsworth expedition. The exploring party, who partook at least once daily of fresh meat in the form of bear's flesh, enjoyed perfect health; while those who remained on board their ship, though taking their doses of lime juice every day, suffered without exception from scurvy, of whom two died. But it is to be remembered that they frequently remarked on the decidedly "high" or "gamey" taste and smell of the meat when the barrels were opened, and they could not be induced to eat fresh bear's flesh on account of its coarseness and peculiar flavor.

In fact, whatever else they had, the meat contained more or less of the ptomaines; while their comrades on land, though with less variety and without any lime juice or other reputed antiscorbutics, did not suffer from ptomaine poisoning, the flesh on which they mainly subsisted being perfectly fresh. So, too, Nansen and Johannsen did not suffer in the least during their sixteen months' solitary sojourn in Franz Joseph Land, though they had no vegetable food whatever, and, unlike the exploring party of Harmsworth's expedition, lived entirely on the flesh of the bears they killed; and we may assume that the crew of the Eira would have enjoyed no less freedom from scurvy without having had forced on them the repulsive draughts of raw blood. Nansen's crew, on the other hand, being for three

whole years, whether free or ice-bound, on the high seas, had no opportunity of obtaining fresh meat, but were entirely exempt from scurvy, thanks to the excellent preservation of their food.

Like Nansen himself and his companions, the members of Leigh Smith's expedition, twenty-five in number, who were wrecked on Franz Joseph's Land in 1881, and wintered there under the most miserable conditions, subsisting for a whole year on a diet exclusively of fresh and often raw flesh, maintained their health to the last.

The peasants in Russian Lapland, though able to obtain farinaceous, saccharine, and vegetable foods, suffer much from scurvy, for the fish which constitutes the nitrogenous part of their diet is generally more or less tainted, from imperfect preservation in winter and from an acquired preference for the taste of "high" fish in summer.

In short, the whole theory of the possession by any foods or drugs of anti-scorbutic properties as such is a delusion. No food, if perfectly free from incipient putrefaction, whether it be fresh or preserved in an aseptic state, will cause scurvy; nor under such conditions will hardship, exposure to cold, depressing mental surroundings, or physical discomfort conduce thereto. On the other hand, incipient putrefaction, if it be so far advanced as to produce any change in the flesh perceptible to the taste or smell, will certainly—and even if it be not may sooner or later—give rise to that form of chronic ptomaine poisoning known as scurvy.

The etiology of infantile scurvy or scurvy rickets (Barlow's disease) is not touched on by Mr. Koettlitz, and does not at first sight seem to admit of so simple an explanation; but since it never occurs in infants at the breast, it is not unreasonable to assume that ptomaines of a kindred nature may be produced in artificial foods by the bacteria in the milk with which these foods are prepared.

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